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Fig. 1A

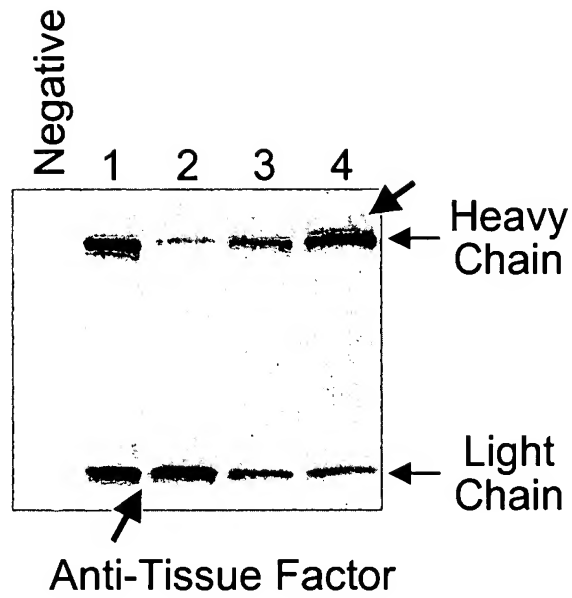


Fig. 1B

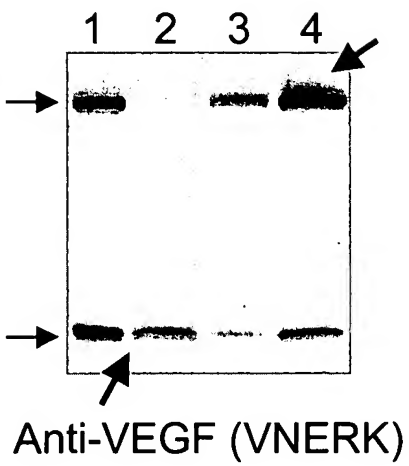


Fig. 2

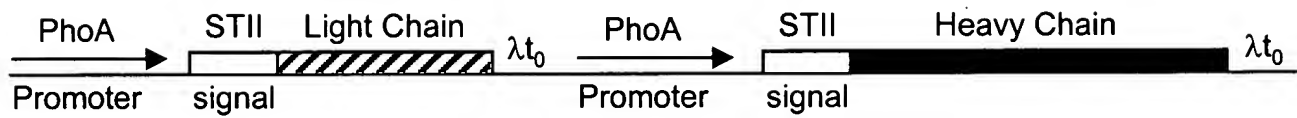


Fig. 3A

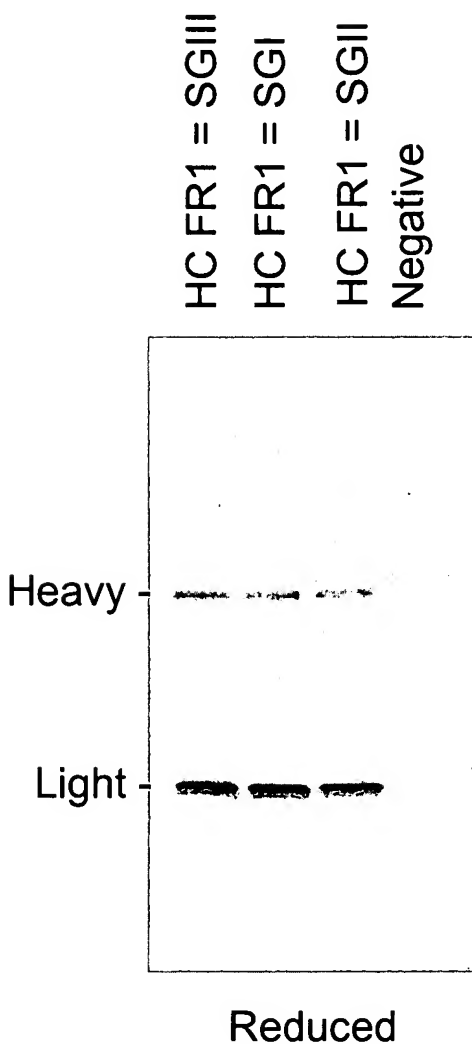


Fig. 3B

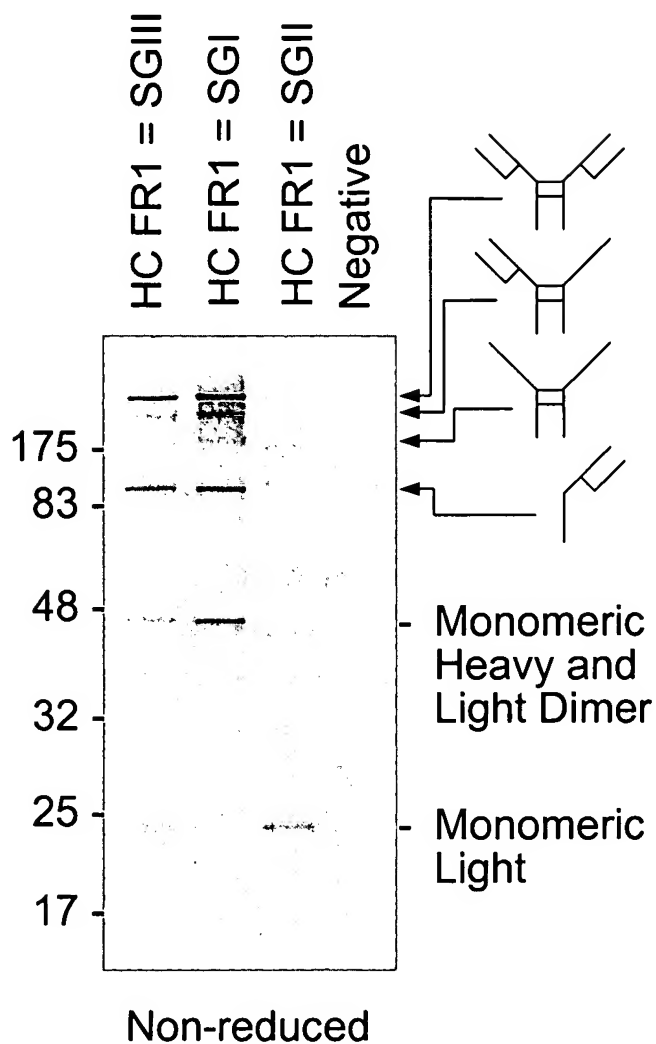


Fig. 4A



Fig. 4B

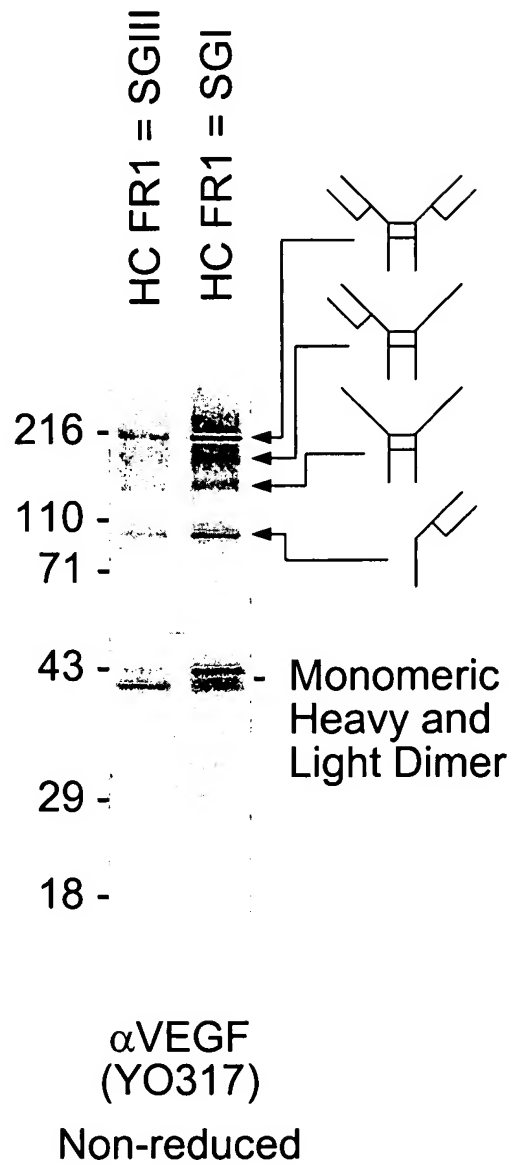


Fig. 5A

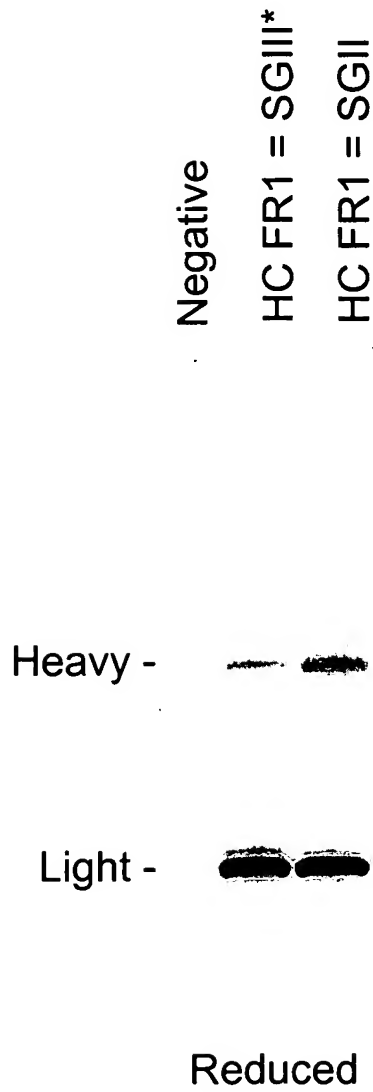
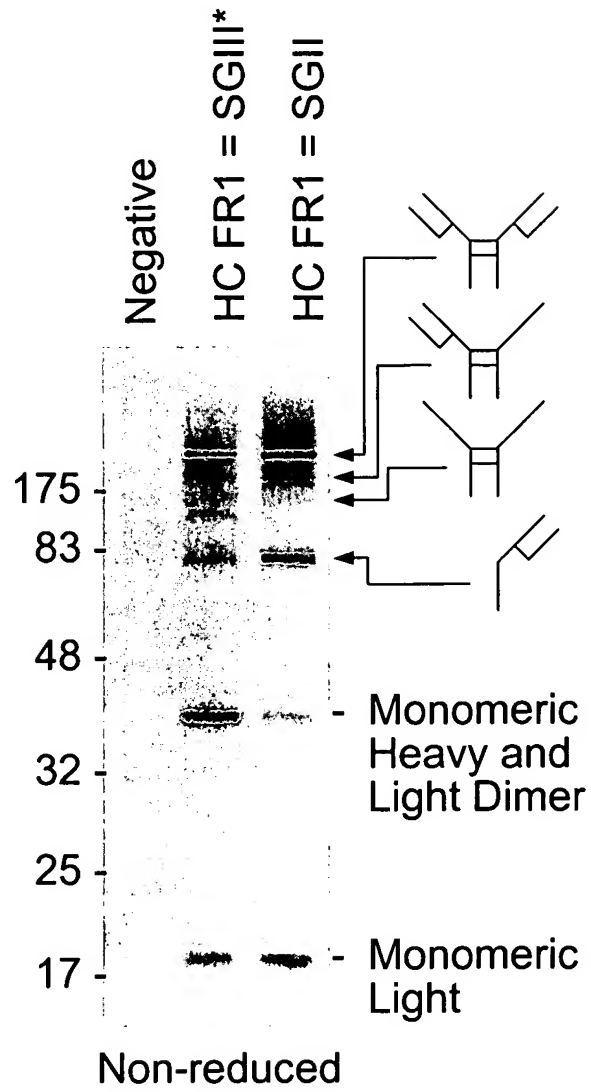


Fig. 5B



*Includes an A24V change as part of humanization.

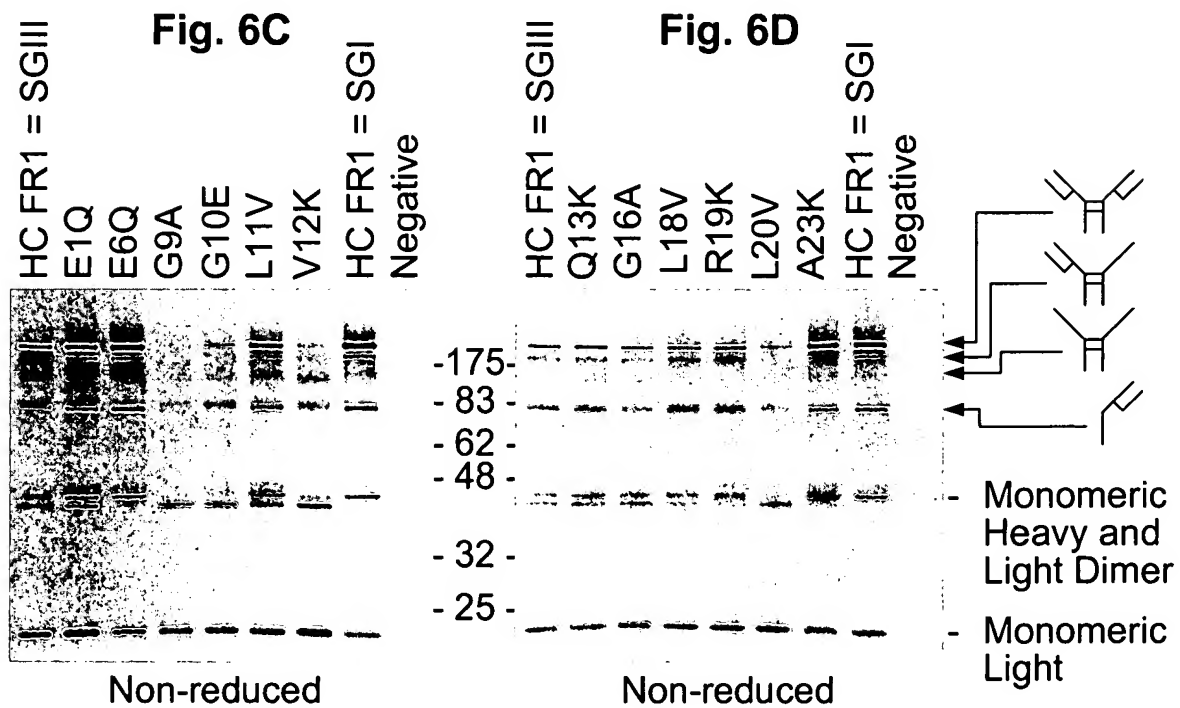
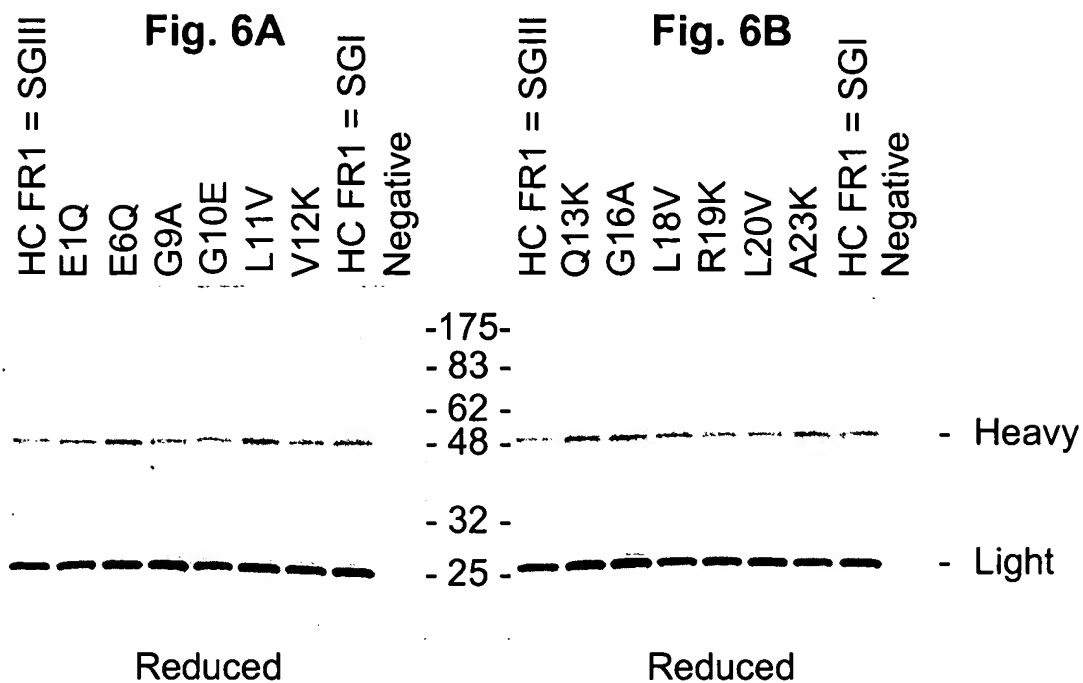


Fig. 7A

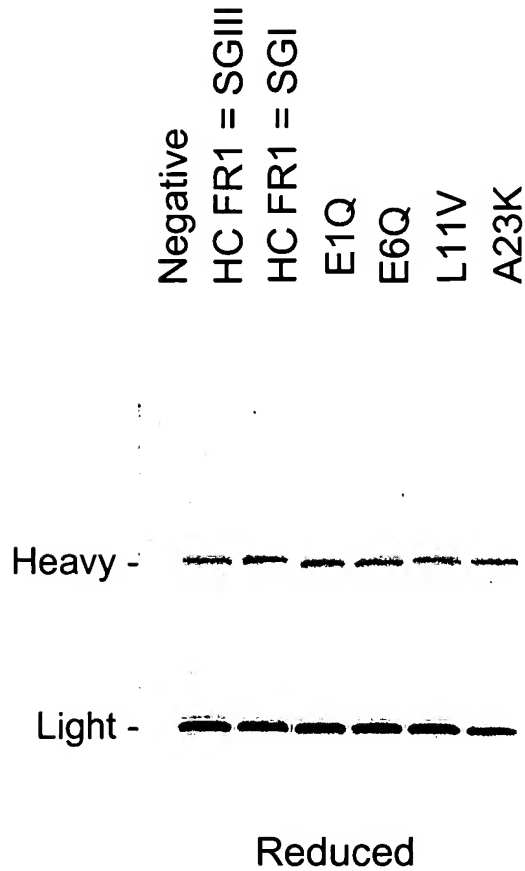


Fig. 7B

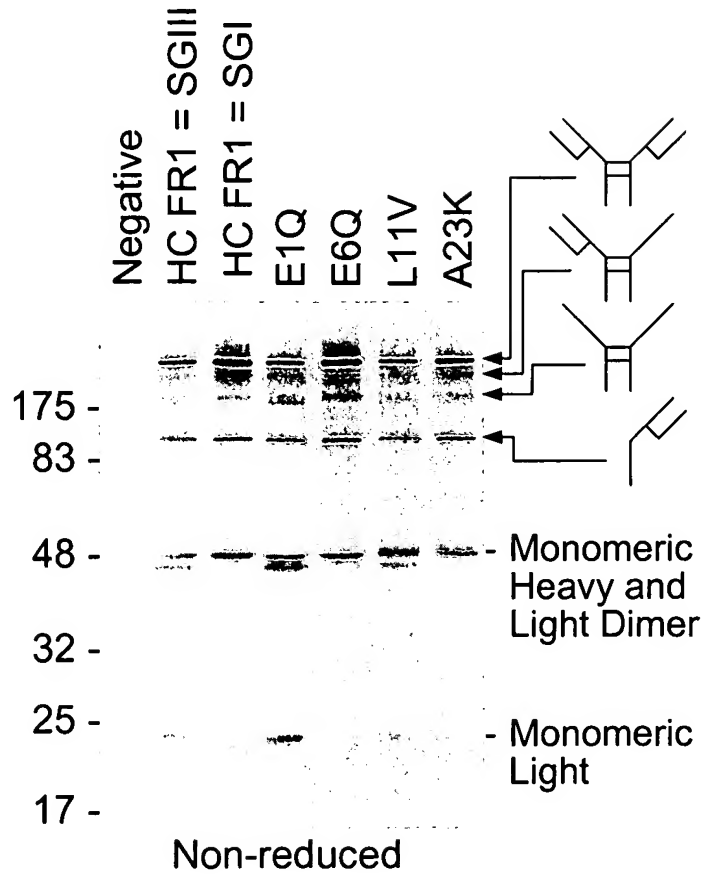


Fig. 8A

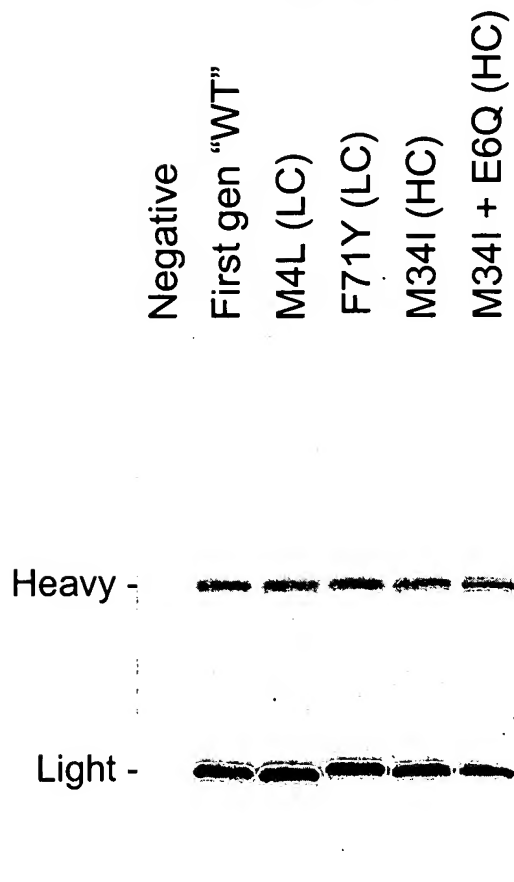


Fig. 8B

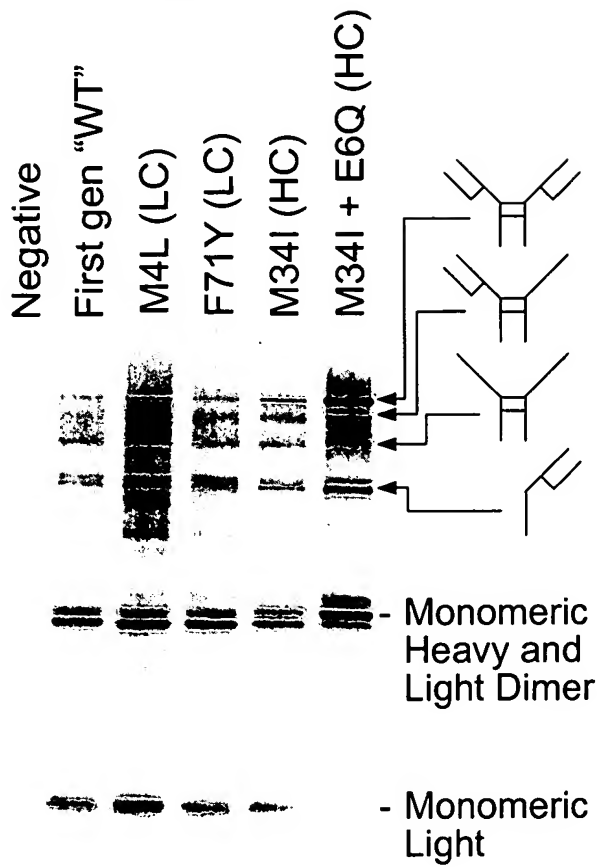


Fig. 9A

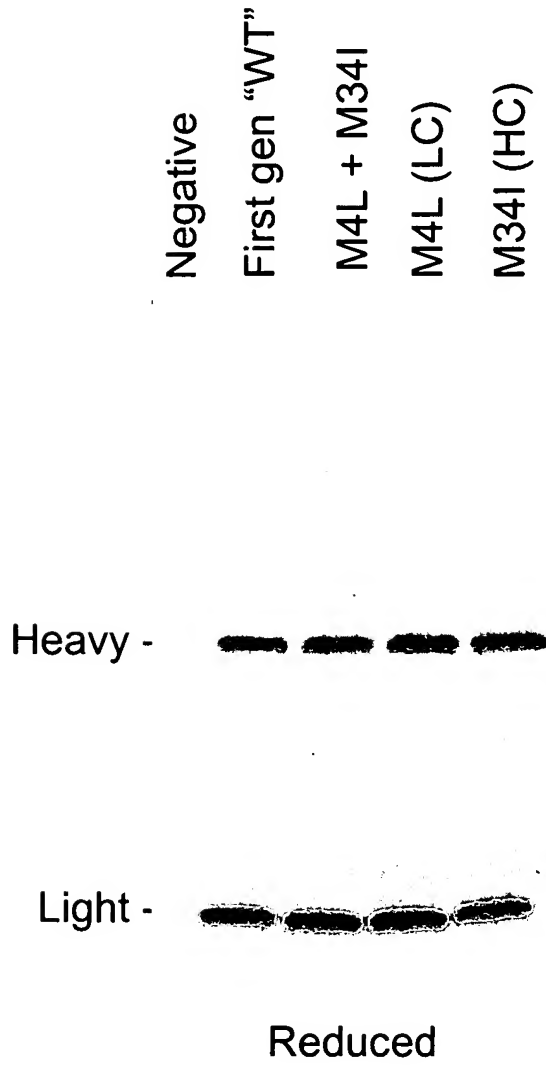


Fig. 9B

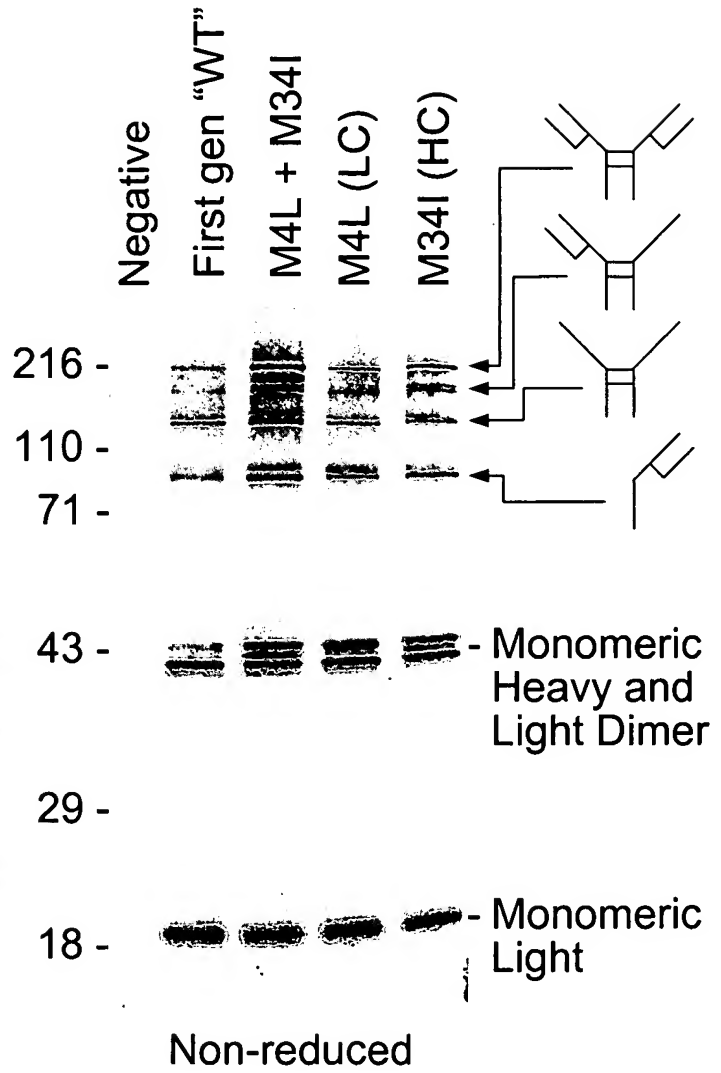


Fig. 10A

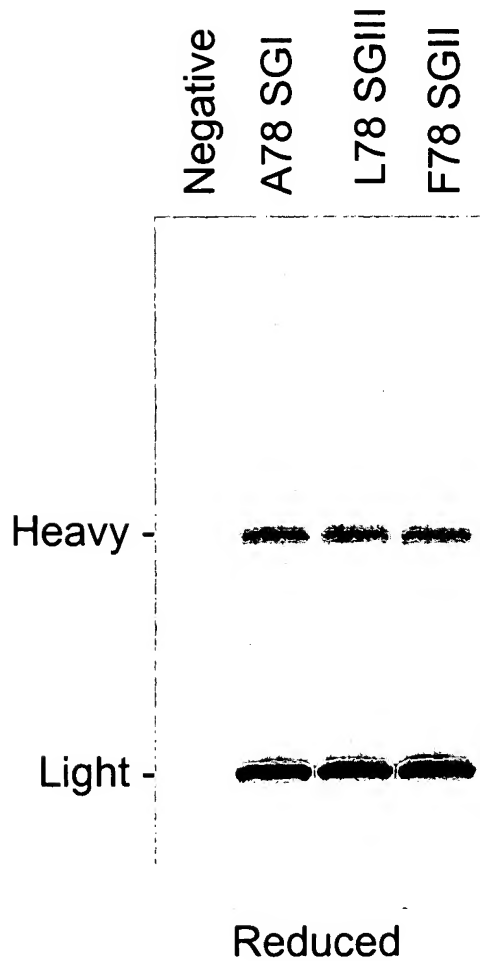


Fig. 10B

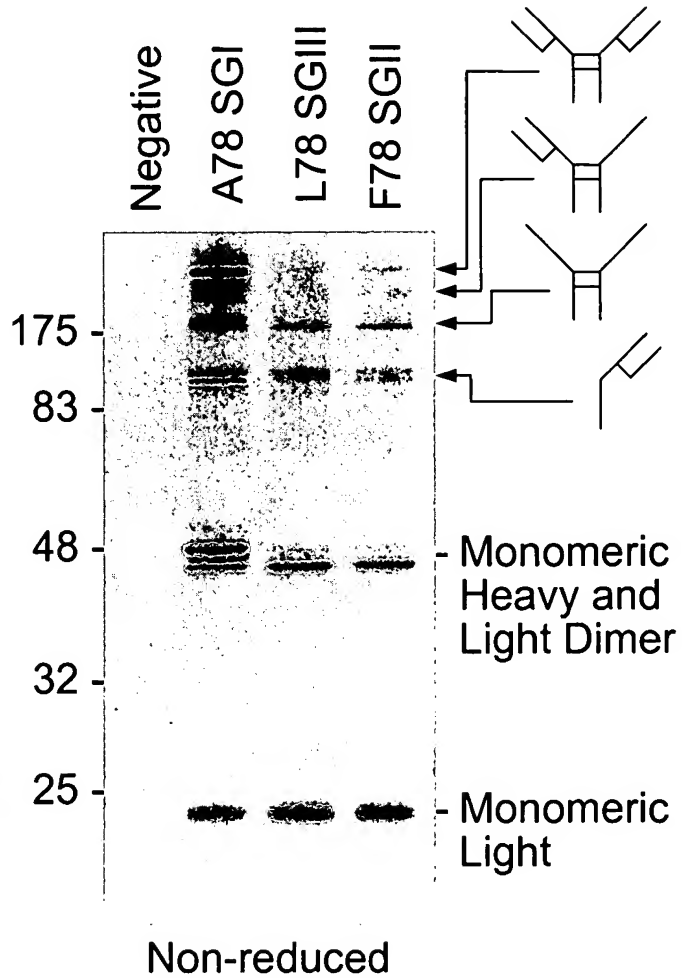


Fig. 11A

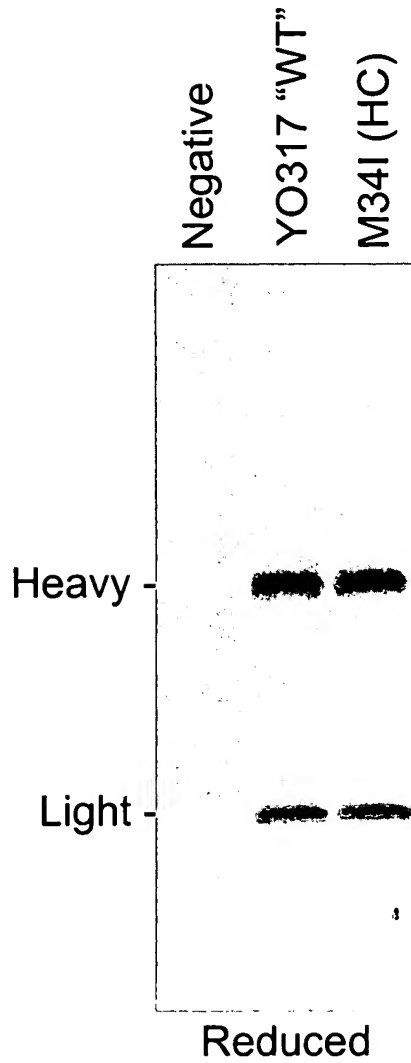


Fig. 11B

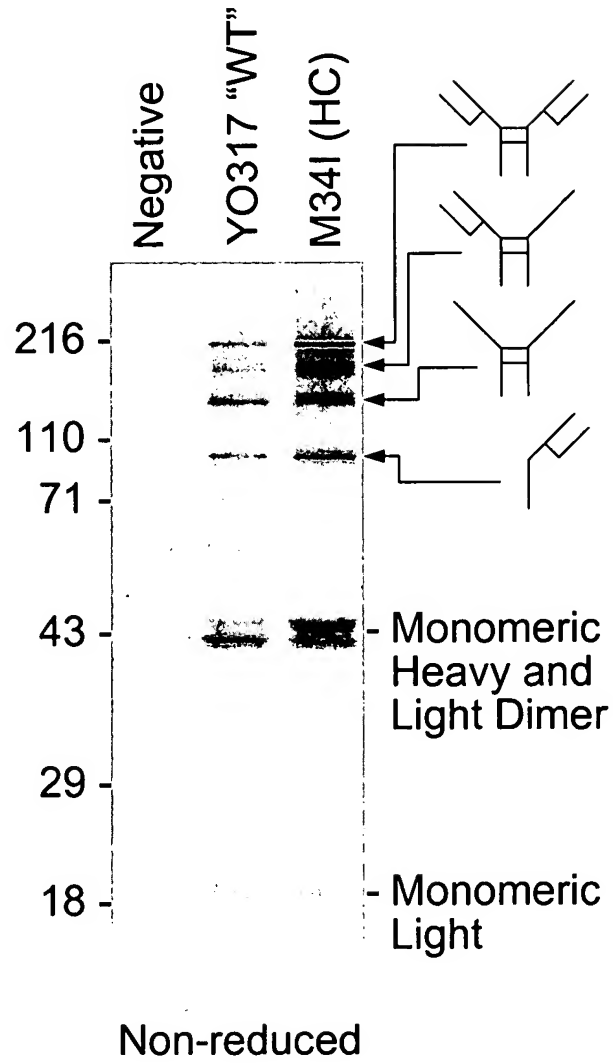


Fig. 12A

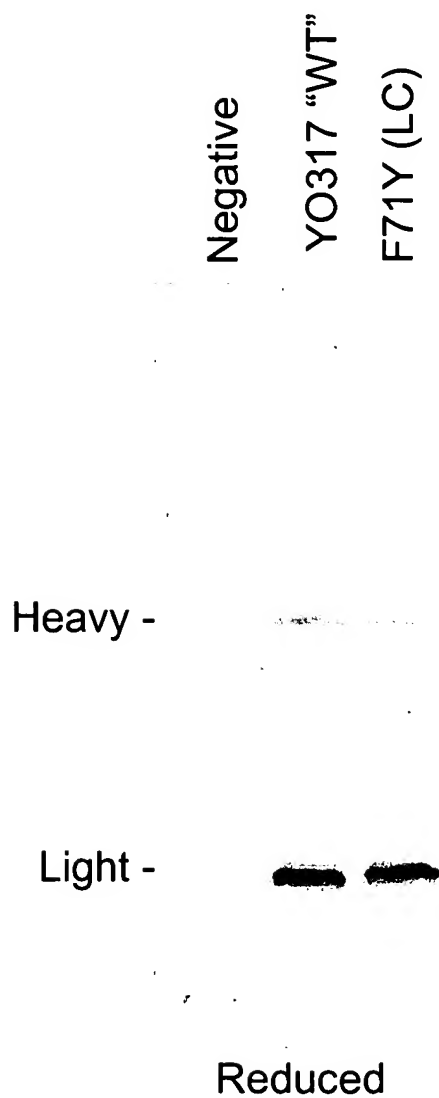
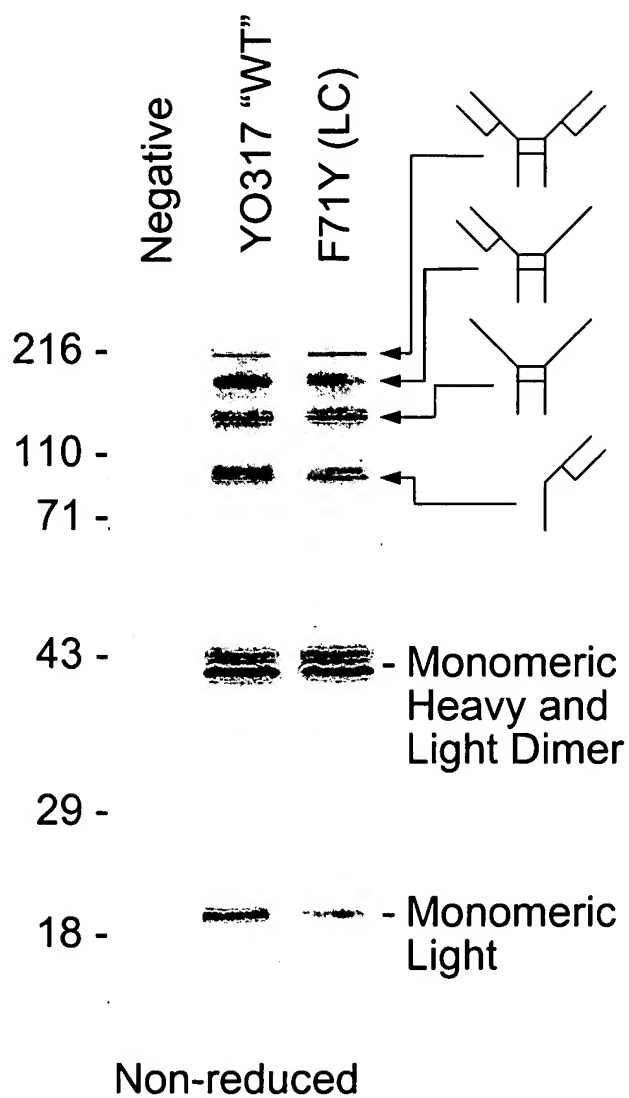


Fig. 12B



* Except for residues changed during humanization.

Fig. 14A

Fig. 14B

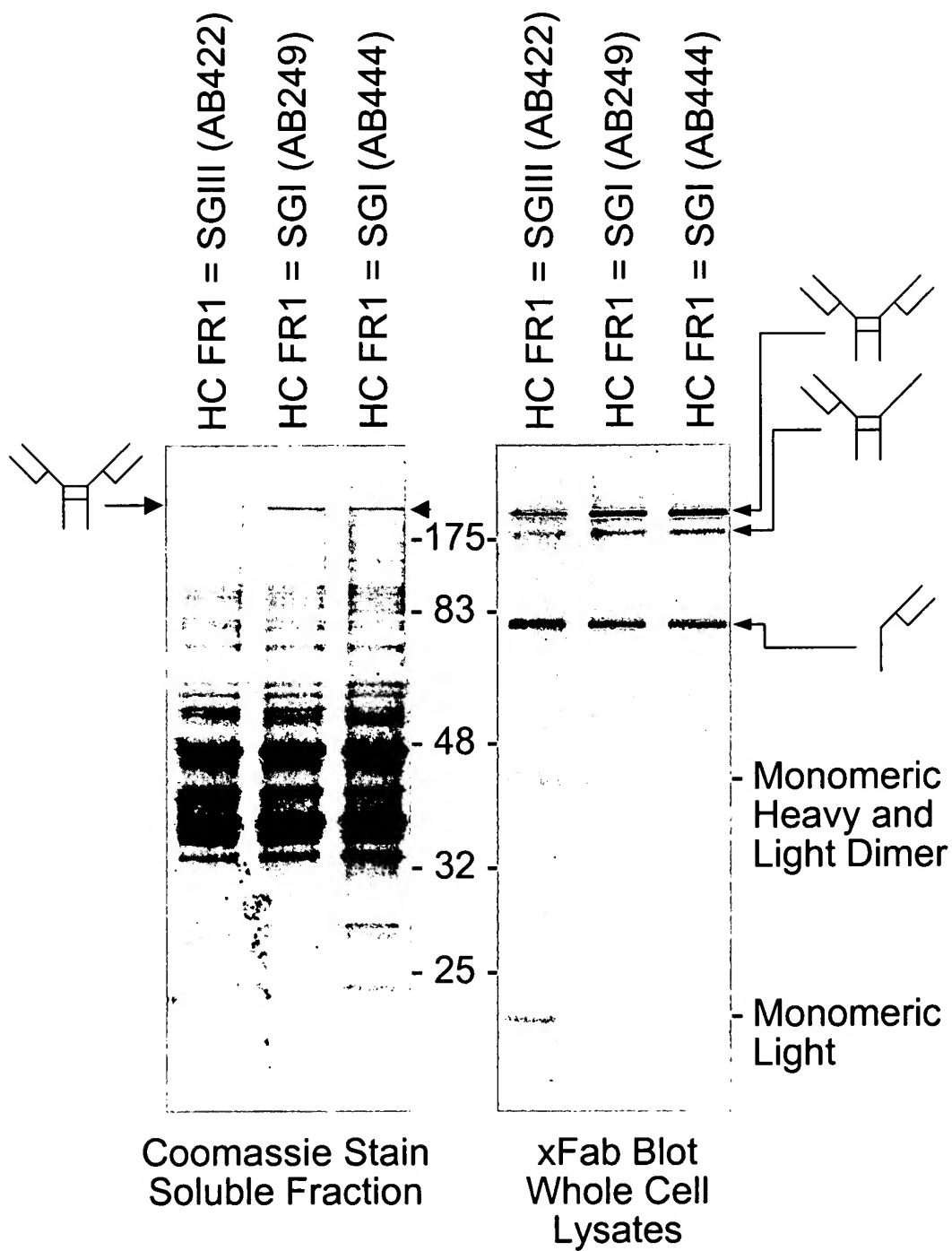


FIG. 15A

1 GAATTCAACT TCTCCATACT ITGGATAAGG AAATACAGAC ATGAAAAATC TCATTGTCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CITTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTATG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTCTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTGTGAG ATTATCGTCA CTGCAATGCT TGGCAATATG GGCAGAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CITTAGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTACGA AGGTTATAC CCGGTTTTAC TGGTTGTGCG CAACTAACATA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATACG GAGCTGTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAFAA AGTGTCAAG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTG GAAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTCCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGCTA CGCTGATATC
AGTGCAATTT TCCCATAGAT CITTAATACTT CTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTCGCGAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGAG CTCCTGTTC GCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
GTCNACTGGG TCAGGGGCTC GAGGACAGG CCGAGACACC CCGTATCCCA GTGGTAGTGG ACCTCGCGTT CAGTCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
^variable light (VL) cys

601 ATCAACAGAA ACCAGGAATA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAC
TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCGAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCAATATCG TGGCACGGCA CCTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
^Variable light cys

801 AAGGTGGAGA TCAAAACGAAC TGTGGCTGCA CCACTGTCTT TCACTTTCCC GGCATCTGAT GAGCAGTTGA AATCTGGNAC TGCTTCTGTT GTGTGCCTGC
TTCCACCTT AGTTTGTCTG ACACCGAGT GGTAGACAGA AGTAGAAGGG CGGTGACTTA CTGCTCAACT ITAGACCTTG ACGAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
Constant Light cys^

FIG. 15B

```
901 TGAATAACTT CTATCCGAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGTAACATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTAATTGAA GATAGGGTCT CTCCGGTTTC ATGTACCTT CCACCTATTG CGGAGAGTTA GCCCAATTGAG GGTCTCTTCA CAGTGCTCG TCCTGTGCTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT AGGAGAAACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC
    CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGAGC CATCTGTGGC AGCTCGGTAC CCGGGGATCT AGGCCTAACG
    AGCGGGCAGT GTTCTCGAA GTTGTCCTCT CTCACAATTA ATTTAGAGA TCGCGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
    ^cys to bind heavy
    ^start lambda t0 terminator^
1201 CTCGGTTGCC GCGGGGCGTT TTTTATTGTT GCGACGGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAAACGG CGGCCCGCAA AAAATAACAA CGGCTGGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
    ^end lambda t0 terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
    GCGTTATACC GCGTTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCCC CCGCGACATG CTCCATTTTC GGCTACGGTC GTAAAGGACTG CTGCTATGCC
1401 AGCTGCTGGC CGATTACGTA AGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACAGG CCGAGACTTA
    TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCITT GTTTTATT TTGTAAGTAT TTGTAAGTAT TACGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAATTTT CCATAGATC TTAATACCTT TTCTTATAGC GTAAAGAGA
    M K K N I A F L L
    ^STII Signal TIR-1
1601 TGCACTATG TTCGTTTTTT CTATTGCTAC AAACGGCTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGGG CTCACCTCGT
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTGCGCATG CGACTCCAAG TCGACCACT CAGACCGCA CCGGACACG TCGGTCCCC GAGTGAGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
    ^anti-VEGF heavy chain (VNERK version)
1701 TTGTCCTGTG CAGCTTCTGG CTATACCTTC ACCAACTAG GTATAAATG GGTCCGTGAC GCCCGGGTA AGGGCCTGGA ATGGGTTTGA TGGATTAAACA
    AACAGGACAC GTCGAAGACC GATATGGAAG TGGTTGATAC CATATTTGAC CCAGGCGCAT TCCCGGCCAT TCCCGAACCT TACCCAACT ACCTAATGT
43 L S C A A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys
1801 CCTATACCGG TGAACCGACC TATGCTGCGG ATTTCAAAG TCGTTTCACT TTTTCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
    GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAGTGA AAAAGAAATC TGGGAGGTT TTGCTGTGCT ATGGACGCTCT ACTTGCGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
```

FIG. 15C

1901 GCGCGCTGAG GACACTGCGG TCTATTACTG TGCAAAAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGGTATT TCGACGTCTG GGGTCAAGGA
CGCGGACTC CTGTGACGGC AGATAATGAC ACGTTTCATG GCGGTGATTA TACACTTGCT CGCCTTCTCG GTGACCATTA AGTGCAGAC CCCAGTTCTT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCCTGGTCA CCGTCTCCTC GGCCTCCACC AAGGGCCCCAT CCGTCTTCC CCTGGCACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCGCTGGGCT
TGGGACCAGT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAGAAGGG GGAACCGTGG AGGAGTTCT CGTGGAGACC CCGTGTGCG CGGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTTC CCGGAACCGG TGACGGTGTG GTGGAACCTA GCGGCCCTGA CCAGCGGCGT GCACACCTTC CCGGCTGTCC TACAGTCTCTC
CGGACCAGTT CCTGATGAAG GGGCTTGGCC ACTGCCACAG CACTTGAGT CCGCGGGACT GGTGCGCGCA CGTGTGGAAG GGCCGACAGG ATGTCAAGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCCTCAGCA GCGTGGTGAC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCGAG CAACACCAG
TCCTGAGATG AGGAGTGTGT CGCACCACTG ACACGGGAGA TCGTCGAACC CGTGGGTCTG GATGTAGAG TTGCACITTAG TGTTCGGGTC GTTGTGGTTC
210 G L Y S L S V V T V P S S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGGACAAGA AAGTTGAGCC CAAATCTTGT GACAAAACTC ACACATGCCC ACCGTGCCCA GCACCTGAAC TCCTGGGGGG ACCGTCAATC TTCTCTTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTTGTTTGG TGTGTACGGG TGGCAGGGGT CGTGGACTTG AGGACCCGCC TGGCAGTCAG AAGGAGAAGG
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCAAAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTGACA TGGTGTGGTG TGGACGTGAG CCAGGAAGAC CCTGAGGTCA AGTTCAACTG
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCTTGGG ACTCCAGTGT ACGCACCCACC ACCTGCACCTC GGTGCTTCTG GGAATCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys

2501 GTACGTGJAC GGCCTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCAGTAC CAGTGTGGTCA GCGTCTCTAC CGTCTGTGAC
CATGACCTG CCGCACCTCC ACGTATTACG GTTCTGTTTC GGGGCCCTCC TCGTCATGTT GTGTGTCATG GCACACCACT GCGCAGGAGTG GCAGGACCTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
^CH2 cys

2601 CAGGACTGGC TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAAG CCTCCAGCC CCCATCGAGA AACCATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGTGACG ACTTACCGTT CCTCATGTT CCGTGTGTTG GGTGTTTTC GGTGAGTCTT TTTGGTAGAG GTTTCGGTTT CCGTGTGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACCAACA GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACCAAGTCA GCGTACCTG CCGTGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGTGG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTCTCACT CCGACTGGAC GGACCACTTT CCGAAGATAG GGTCTGCTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 15D

```
2801 CGCGTGGAG TGGGAGGCA ATGGGAGGC GGAGAACAAC TACAAGACA CGCTCCCGT GCTGGACTCC GAGGGCTCCT TCTTCTCTA CAGCAAGCTC
    GCGCACCTC ACCTCTCGT TACCGTCCG CTTCTTGTTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGG AGAAGGAGAT GTCGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGACGAGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAAGA GTACGTAATC CTACGTACTC CGAGACGTGT TGGTGATGT CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCGGGGGG TTTTATTG TTAACATATG TTTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCGTACG CTGCCGGGAT CTCAGGGATT GCGAGCCCAAC GCGCGCCCGC AAAAAATAAC AATTGAGTAC AAACGTGTCA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator
    ^start of tet resistance promoter ^start of tet resistance promoter
    ^-10 region of tet resistance promoter ^-35 of promoter
3101 AAGCTTTAAT GCGGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCGTCTCAT CGTCATCCTC GGCACCGTCA
    TTGGAATTA CGCCATCAA TAGTGTCAAT TTAACGATTG CGTCAGTCCG TGGCACATAC TTTAGATTGT TAGCGGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGTTA TGCCGGTACT GCGGGGCCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCAGCA
3301
```

FIG. 16A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTATT TT AGCTTGCCC AAAAAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATCTG TACTTTTAG AGTAACGACT CAACAATAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACTGTGTG CGCAGGTAGA AGCTTTGAG ATPATCGTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTGCG CAACTAATA GTCCATCTCC

201 GGGGGCTGTA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATAGG GAGCTGTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTGTCCAGG GCGGAGCTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAATA GTACGCCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCAGGTAAA AGGTATCTA GAATTATGAA GAAGAATATC GAATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCAITTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAAG AAGCTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1 Anti-VEGF Light chain (version Y0317)^

501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCC GCTCTGTGG GCGATAGGTT CACCATACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
GTCAACTGGG TCAGGGGCTC GAGGACACAG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACCTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAAA GCTCCGAAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCGTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGAATTTCACT CTGACCATCA GCAGTCTGCA GCAGAAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGAGGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCTATCG TGGCAGCGCA CCTGCAAAAC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGCG
TTCCACCTCT AGTTGTCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACCAAGACAA CACACGGAGG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCCAGA GAGGCCAAG TACAGTGGAA GGTGGATAC GCCTCTCCAT CCGGTAATCT CCAGGAGAGT GTACACAGAGC AGCACAGCAA
ACTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTAG GGTCTCTCA CAGTGTCTCG TCCGTGCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 16B

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAGAAACA CAAAGTCTAC GCGTCGGAAG TCACCCATCA GGGCCTGAGC
CCTGTCGTGG ATGTCGAGT CGTGCTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGACGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCTCTT AGCCCGGAGG CATCTGGGTAC CCGGGGATCT AGGCCTAAGG
AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTACAAATTA ATTAGGAGA TCGCGCCTGC GTAGCACCGC TCAGGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGT TTTTATTGT GCGGACGCG ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCCAC TGCAATGCTT
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACATTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
GCCTTATACC GCCTTTTACT GGTGTGCGC AACTAATAG TCCATCTCCC CCGGACATG CTCATTTCCG GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTCACACAG CTGTCATAAA GTTGTACGG CCGAGACTTA
TCGACGACGC GCTAATGCA TTTCTCAATA ACTTCGTAGG AGCAGTCAIT TTTCAAATAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTGAATGTAT TTGTAAGTAG TAGCAAGTT CAGTAAATAA GGTATCTTAG AATTATGAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCCATAGATC TTAATATCTT TTCTTATAGC GTAAAGAAGA
1
1601 TGCACTATG TTGCTTTTCTT CTATTGCTAC AAACGCGTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCTGGTGC AGCAGGGGG CTCACTCGGT
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTCGCGCATG CGACTCCAAG TCAGCCACTT CAGACCGCCA CCGGACCAGG TCGGTCCCC GAGTGAGGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^Anti-VEGF Heavy Chain (version Y0317)
1701 TTGTCCTGTG CAGCTTCTG CTAGACITC ACACACTAG GTATGAATG GTTCGTGAG GCGCCGGTA AGGCGCTGGA ATGGGTTGGA TGGATTAAACA
AACAGGACAC GTCGAAGACC GATGCTGAAG TGGTGTGATG CATACTGAC CCAGGCGCAT CCGGGCCCAT TCCGGGACCT TACCAACCT ACCTAATGT
43 L S C A A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCG TGAACCGACC TATGCTGCG ATTTCAAAG TCGTTTCACT TTTCCTTTAG ACACCTCCA AAGCACAGCA TACCTGCAGA TGAACAGCCT
GGATATGGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGGAGTTT TGTGTGCTT ATGACGCTT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGCGCTGAG GACACTGCC TCTATTACTG TGCAAGTAC CCGTACTATT ATGSGACGAG CCACTGGTAT TTCGACGTCT GGGGTCAAG AACCTGGTC
CGCGGACTC CTGTGACGCG AGATAATGAC ACGTTCATG GGCATGATAA TACCTGTCTC GGTGACCAATA AAGTGCAGA CCCAGTTCC TTGGGACCAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCTC CGGCCTCCAC CAAGGGCCCA TCGTCTTCC CCCTGGCACC CTCTCCAG AGCACCTCTG GGGCACAGC GGCCTTGGC TGCTTGTCA
TGGCAGAGGA GCGGAGGTG GTTCCCGGT AGCAGAAGG GGGACCTGG GAGGAGTTTC TCGTGGAGAC CCCGTGTG CCGGAGCCG ACCGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K
^STII Signal TIR-1
M K K N I A F L L

FIG. 16C

2101 AGGACTACTT CCCGAACG GTACGGTGT CGTGGAACTC AGGCGCCCTG ACCAGCGCG TGCAACACTT CCGGCTCTC CTACAGTCT CAGGACTCTA
TCTCTATGAA GGGGCTTGGC CACTGCCACA GCACCTTAG GCACCGGAC TGGTCGGCG ACCTGTGGAA GGGCCGACAG GATGTGAGG GTCTTGAGT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCTCAGC AGCGTGGTA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CTTACATCTG CAACTGTAAT CAAAGCCCA GAAACACAA GGTGGACAAG
GAGGAGTCTG TCGCACTACT GACACGGGAG ATCGTCGAAC CCGTGGTCT GATGTAGAC GTTGCACTTA GTTTCGGGT CGTGTGGT CCACCTGTTC
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGCC CACCTGCC CACCTGCTGAA CTCTGGGG GACCGTCACT CTCTCTCTC CCCCCAAAC
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACGG GTGGCACGG TCGTGGACTT GAGGACCCCG CTGGCAGTCA GAGGAGAAG GGGGTTTTG
243 K V E P K S C D K T H T C P A P E L L G G P S V F L F P P K P
2401 CCAAGACAC CCTCATGATC TCCCGACCC CTGAGGTAC ATGCGTGGT GTGCACTGA GCCACGAAGA CCTGAGGTC AAGTTCACT GGTACGTGGA
GGTTCCTGTG GGAGTACTAG AGGSCCTGG GACTCCAGTG TAGGCACAC CACTGCACT CGTGTCTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 OGGGTGGAG GTGCATATG CCAGACAAA GCGCGGGAG GAGCAGTACA ACAGCAGTA CCGTGTGGT AGCTCTCTCA CCGTCTGCA CAGGAGCTGG
GCCGACCTC CACGTATTAC GGTTCGTGT CCGCGCCCTC CTGCTCATGT TGTGTGCAT GGCACACGAG TCGCAGGAGT GGCAGGAGT GGTCTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGCA AGGAGTACAA GTGCAAGTTC TCCAAACAA GCGTCCAGC CCGTCCAGT CCAACCATCT CCAAGCCAA AGGCGAGCC CGAGAACCAC
GACTTACCGT TCCTCATGTT CAGTTCAG AGTTCGTTC GGGAGGCTG GGGTAGCTC TTGTGTAGA GGTTCGGTT TCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CCTGCCCCA TCCCGGGAAG AGATGACCAA GAACAGGTC AGCTGACCT GCTGTGTCAA AGCTTTCTAT CCAAGCACA TCCCGGTGGA
TCCACATGTG GGCAGGGGT AGGCGCTTC TCTACTGTT CTGTGTCAG TCGGACTGGA CGGACCACT TCCGAAGATA GGTGCGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGGAGC AATGGGAGC CGGAGAACA CTACAGACC AGCTCTCCG TCGTGGACT CAGCGCTCC TTCTCTCT ACAGCAAGT CACCGTGGAC
CACCCTCTG TTACCGGTG GCTCTTGT GATGTTCTG GATGTTCTG TCGGAGGCG AGACCTGAG GCTGCGAGG AGAAGGAGA TGTCTTGA GTGGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGT GGCAGAGGG GAAGTCTTC TCATGCTCG TGAATCATGA GGCTCTGAC AACCACTACA CGCAGAAG CTTCTCCCTG TCTCCGGTA
TTCTCTCCA CGTCTGCC CTTGCAGAAG AGTACGAGC ACTACGTACT CCGAGAGTG TTGGTCACT GGTCTCTC GGAGAGGAC AGAGGCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAAGCATG CGAGCGCCT AGATCCCTA AGCTCGGT GCGCGGGG GTTTTTTAT GTTAATCAT GTTTGACAGC TTATCATGA TAAGCTTAA
TTATCTGTAC GCTGCCGGA TCTCAGGAT TCGAGCCAA CGGCGGGCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGT ATTGAAAT
477 O
3101 TGGGTAGT TATCAGTT AATTGCTAA CGCAGTCAG CACCTGTAT GAAATCAAC AATGCGCTA TCGTCATCT CGGCACGTC ACCCTGATG
ACCCATCAA ATAGTGTCA TTTAACGAT GGTGAGTCC GTGGACATA CTTAGATTG TTAGCGAGT AGCAGTAGA GCCGTGGAG TGGACCTAC
*Start Tet Resistance Coding Sequence

FIG. 16D

3201 CTGTAGGCAAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCTT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTCTGTA GCGGTCAGTG ATACCGCAGG ACGATCGCGA

3301

FIG. 17A

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1 GAATTCAACT TCTCCATAC TTTGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTCTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTGCG CAACTAAC TA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGGATGCCA GCATTCTTGA CGACGATAGG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGG CGCTAATGCA TTCTTCAAT AACCTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAGG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTCC CGGCTCTGNA TATCAGCGNA ACAAAATAA AAATTTACAT AACATTGAT CATGCGTTCA

401 TCAGTAAAG AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGTGTATATC
AGTGCATTTT TCCCATAGAT CTTAATACIT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCGGAG CTCCTGTGCC GCCTGTGG GCGATAGGTT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCGCTT CAGTCCCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
^variable light (VL) cys

601 ATCAACAGAA ACCAGGAAGA GCTCCGAAGA TACTGAITTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAG
TAGTGTCTTT TGGTCCCTTT CGAGGCTTTT ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTATATCG TGGCAGCGCA CTGCAAAACC TGTCCCATGG
93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
^Variable light cys

801 AAGGTGGAGA TCAACGAAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTTGT GTGTGCTGTC
TTCCACCTCT AGTTTGTCTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA CACACGAGC
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
Constant Light cys^

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FIG. 17B

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901 TGAATAAATT CTATCCAGA GAGGCCAAG TACAGTGAA GGTGGATAAC GCCCTCCAAT CGGTAAATC CCAGGAGAGT GTACACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACTTT CCACCTATTG CCGGAGGTTA GCCCATTTAG GGTCTCTTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAGCAGAGT ACAGAGAAAC CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC
CCTGTCTGTG ATGTCTGAGT CGTCTGCGA CTGCGACTCG TTCTGTCTGA TGCTCTTTGT GTTTCAGATG CCGACGCTTC AGTGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
^Constant Light cys

1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGA GAGTGTTAAT TAAATCCTCT ACGCGGAGC CATCTGGCG AGCTCGGTAC CCGGGATCT AGGCCTAAGC
AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGGAGA TCGGCGCTGC GTAGCACGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
^cys to bind heavy start lambda to terminator^

1201 CTGGTTGCC GCGGGGGT TTTTATTGTT GCGGAGGCG ATCTCGAATG AACTGTGTG GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
GAGCCAAAGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTACGAA
^end lambda to terminator

1301 CGCAATATGG CGCAAAATGA CCAACAGCG TTGATTGATC AGGTAGAGGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
CGTTATATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTG GGTACGGTC GTAAGGACTG CTGCTATGCC

1401 AGTGTCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCTATAA GTTGTACGG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTCTGAAT

1501 TAGTCTCTTT GTTTTATTT TTAAATGAT TTGTAAGTAG TAGCAAGTT CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAATAAAA AAATTACATA AACATTGATC ATCGGTTCAA GTGCAATTTT CCCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
M K K N I A F L L
^STII Signal TIR-1

1601 TGCATCTATG TTGGTTT TTTTCTTTT CTATTGCTAC AAACGGCTAC GCTCAGGTTG AGCTGGTGCA GTCTGCGCA GAGGTGAAAA AGCCAGGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAAA GATAACGATG TTGCGCATG CGAGTCCAGT TCGACACAGT CAGACCGCGT CTCCACTTTT TCGGTCCCG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
^anti-VEGF Heavy Chain (VNERK version)
^Heavy Chain FR1 changed to Subgroup I consensus sequence

1701 GTATCTGTA AAGCTTCTGG CTATACCTTC ACCAATATG GTATAAATG GGTCCGTGAG GCGCCGGTA AGGCGCTGGA ATGGTTGGA TGGATTAAAC
CATAGGACAT TTCGAAGACC GATATGGAAG TGGTTGATAC CATATTTGAC CCAGCGAGTC CCGGGCCCAT TCCCGACCT TACCCAACT ACCTAATTT
43 V S C K A S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
^Variable Heavy (VH) cys

1801 CCTATACCG TGAACGACC TATGCTGGG ATTTCAACG TCGTTTCACT TTTTCTTTAG ACACCTCCAA AAGCAGAGCA TACCTGCAGA TGRACAGCCT
GGATATGGCC ACTTGCTGG ATACGAGCC TAAAGTTGCG AGCAAGTGA AAAAGAAATC TGTGAGGTT TTCGTGTCTG ATGGACGCT ACTTGTGGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

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FIG. 17C

1901 GCGGCTGAG GACACTGCG TCTATTACTG TGCAAGTAC CCGCACTATT ATGTGAACGA GCGGAAGAGC CACTGTGTATT TCGACGTCTG GGGTCAAGGA
CGCGGACTC CTGTGACGC AGATAATGAC AGTTTTCATG GCGTGATAA TACACTTGCT CGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCTT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCCTGGTCA CGCTCTCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CTGGGACCC TCCTCCAAGA GCACCTCTGG GGGCACAGCG GCCCTGGGCT
TGGACCCAGT GGCAGAGGAG CCGGAGGTGG TTCCCGGGTA GCCAGAAGGG GGACCGTGGG AGGAGTTCT CGTGGAGACC CCCGTGTGCG CGGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTC CCGAACCGG TGACGGTGTG GTGGAACCTCA GGGGCCCTGA CCAGCGGGGT GCACACCTTC CCGGTCTCTC TACAGTCTTC
CGGACCCAGT CCGATGAAG GGGCTTGGCC ACTGCCACAG CACCTTGAGT CCGCGGACT GTGCGCGCA CGTGTGAAG GGGCGACAGG ATGTCAAGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCTCTAGCA GCGTGTGAGC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG
TCCTGAGATG AGGAGTCTG CGCACCACTG ACACGGGAGA TCGTCGAACC CCGTGGTCTG GATGTAGAG TTGCACCTAG TGTTCGGGTC GTTGTGTTTC
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGACACAAG AAGTTGAGC CAAATCTTGT GACAAAACCT ACACATGCCC ACGTGCCCA GCACCTGAAC TCCTGGGGG ACCGTCTAGTC TTCCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTTGTTTGG TGTGTACGGG TGGCACGGGT CGTGGACTTG AGGACCCCCC TGGCAGTCAG AAGGAGAAGG
243 V D K K V E P K S C D K T H T C P P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCAAAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTACCA TGGTGTGTGG TGGACGTGAG CCACGAAGAC CCGTGGTCA AGTTCACATG
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCCTGGG ACTCCAGTGT ACSCACCACC ACTGCACTC GTGTCTTCTG GGAATCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys

2501 GTACGTGGAC GGCCTGGAGG TGCATAATGC CAAGACAAG CCGCGGGAGG AGCAGTACAA CAGCACGTAC CGTGTGTGTC GGTCTCTCAC CGTCTCTCAC
CATGACCTG CCGACCTCC ACGTATTACG GTTCTGTTC GGGGCCCTCC TCGTCATGTT TGTGTGATG GCACACCATG CGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

2601 CAGGACTGGC TGAATGGCAA GGAGTACAAG TGCAGGTCT CCAACAAGC CTCTCCAGC CCCATCGAGA AAACATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTT CCGTCCAGA GTTGTGTTG GAGGGGTGG GTGTAGTCT TTTGGTAGAG GTTTCGGTTT CCCGTCCGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACCAAC GGTGTACACC CTGCCCCCAT CCGGGGAAGA GATGACCAAG AACCAAGTCA GCTGTACTG CCTGGTCAA GGTCTCTATC CCAGCGACAT
CTCTTGGTGT CCACATGAG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTCTCAGT CGGACTGAC GGAACAGTTT CCGAAGATAG GGTCTGTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 17D

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2801 CGCGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCTCCCGT GCTGGACTCC GAGGCTCCT TCTTCTCTA CAGCAAGCTC
    GCGCACCTTC ACCTCTCGT TACCCGTGGG CCTCTTGTTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
    TGGCACCTGT TCTCGTCCAC CGTCGTCCCC TTGCAGAGA GACAGGAGCA CTACGTACTC CGAGACGCTG TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
    ^CH3 cys
3001 CTCGGGGTAA ATAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CCGCCGGGCG TTTTATTG TTAAGTATG TTGACAGCT TATCATCGAT
    GAGGCCCAT TATTCGTACG CTGCCGGAT CTCAGGGATT GCGAGCCCAAC GCGGCCCGC AAAAAATAAC AATTGAGTAC AAAGTGTGA ATAGTAGCTA
477 P G K O
    ^start lambda t0 terminator ^end lambda t0 terminator ^start of tet resistance promoter
    ^-35 of promoter
3101 AAGCTTTAAT GCGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGC ACGTGATG AAATCTAACA ATGCGCTCAT CGTCATCCTC GGCACCGTCA
    TTGGAATTA CGCCATCAA TAGTGTCAT TTAACGATTG CGTCAGTCCG TGGCACATAC TTAGATTGT TAGCGAGTA GCAGTAGGAG CCGTGGCAGT
    ^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGTTA TGCCGGTACT GCGGGGCCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTCTC
    GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCTGTAG CGGTCACTGA TACCGCAGCA
3301
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FIG. 18A

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1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
  CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAAGTGTG CCGAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACACAGG GTTGATTGAT CAGGTAGAGG
  CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGGTTACGA AGCGTTATAC CCGGTTTTAC TGGTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAG CCGATGCA GCATTCTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
  CCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACCA GCTGTCTATAA AGTGTCTACG GCGGAGACTT ATAGTCGCTT TGTTTTTTAT TTTTAATGTA TTGTAACTA GTACGCAAGT
  TTTTCAATTA GAAAAGTTGT CGACAGTAAT TCACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
  AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
  1 M K K N I A F L L A S M F V F S I A T N A Y A D I
    ^STII Signal TIR -1 anti-VEGF Light Chain^

501 CAGTTGACCC AGTCCCCGAG CTCCTGTGCC GCGTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TPAAACTGGT
  GTCAACTGGG TCAGGGGCTC GAGGACAGG CGGAGACACC CGGTATCCCA GTGGTAGTGG AGCTGCGGTT CAGTCTCTATA ATCGTTGATA AATTGACCA
  26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y
    ^variable light (VL) cys

601 ATCAACAGAA ACCAGGAATA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTGCTTC TCTGATCCG GTTCTGGAC
  TAGTTGTCTT TGGTCCTTTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCTTG
  60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCGAGAAGAC TTGCGCAACTT ATTACTGTCA ACAGTATAGC ACGGTGCGGT GGACGTTGG ACAGGGTACC
  CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AGCGTTGAA TAATGACAGT TGTCTATCG TGGCACGCA CCTGCAAAACC TGTCCTCATGG
  93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T
    ^Variable light cys

801 AAGGTGGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCGATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCTGTC
  TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CCGTAGACTA CTGGTCAACT TTAGACCTTG AGAAGACAA CACACGGACG
  126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L
    Constant Light cys^
```

FIG. 18B

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901 TGAATAACTT CTATCCAGA GAGGCCAAG TACAGTGAA GTGGATAAC GGCCTCCAAT CGGTAACATC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
    ACTTAITGAA GATAGGTCT CTCCGGTTC ATGTACCTT ACACCTATTG CGGGAGGTTA GGCCTCTCA CAGTGTCTCG TCCTGTCTGT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACAGAAACA CAAAGTCTAC GCCTGGAAG TCACCCATCA GGGCCTGAGC
    CCTGTCGTGG ATGTCGGAGT CGTCGTGGA CTGCGACTCG TTTCGTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTC AGTGGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
    ^Constant Light cys
1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT AGCCCGGAGC CATCGTGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG
    AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGAGA TCGGGCCCTG GTAGCACCGC TCGAGCCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O ^cys to bind heavy
    start lambda to terminator^
1201 CTCGGTTGCC GCGGGCGT TTTTATTCTT GCGAGCGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT
    GAGCCAACGG CGGCCGCAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACAGC CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTAGAA
    ^end lambda to terminator
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGTAGAGGG GGGGCTGTAC GAGGTAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
    CGGTATATACC GCGTTTACT GGTGTGCGC AACTAAGTAG TCCATCTCCC CCGGACATG CTCCATTTCG GGCTACGGTC GTAAGGAGTG CTGCTATGCC
1401 AGTGTCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TGCTCAGTAA AAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA
    TCGAGGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TAGGCAAGTT CAGTAAAAA GGTATCTTAG AATTATGAG AAGAATATCG CATTTCTTCT
    ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATACTTC TTCTTATAGC GTAAAGAAGA
    M K K N I A F L L
    ^STII Signal TIR-1
1601 TGCATCTATG TTCGTTTTTT CTATGCTTAC AAAGCGGTAC GCTCAGGTTC AGTGCAAGA GTCTGGCCCG GGCTGGTGA AACCATCTCA GACTCTCTCC
    ACGTAGATAC AAGCAAAAAA GATAACGATG TTTGCGCATG CGAGTCCAAG TCAGCGTTCT CAGACCGGCG CCGGACCATT TTGGTAGAGT CTGAGAGAGG
10 A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S Q T L S
    ^anti-VEGF heavy chain (VNERK version)
    ^Heavy chain FR1 changed to Subgroup II consensus sequence
1701 TTGACTTGTA CTGTTTCTGG CTATACCTTC ACCAACTATG GTATAAATG GTTCCTGTCAG GCGCCGGGTA AGGCGCTGGA ATGGGTGGA TGGATTAAACA
    AACTGAACAT GACAAAGACC GATATGGAAG TGGTGTGATAC CATATTGAC CCAAGGCAGTC CCGGGCCCAT TCCGGGACT TACCCAACCT ACCTAATTGT
43 L T C T V S G Y T F T N Y G I N W V R Q A P G K G L E W V G W I N T
    ^Variable Heavy (VH) cys
1801 CCTATACGG TGAACCGACC TATGCTGCGG ATTTCAAACG TCGTTTCACT TTTTCTTTAG ACACCTCCAA AAGCACAGCA TACCTGCAGA TGAACAGCCT
    GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAAATGA AAAAGAAATC TGTTGAGGTT TTGTTGTGCT ATGACAGTCT ACTTGTCCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L

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FIG. 18C

1901 GCGGCTGAG GACACTGCG TCTATTACTG TGCAGATGAC CGGCACTATT ATGTGAACGA GCGGAAGAGC CACTGTGTATT TCGACGTCTG GGGTCAAGGA
CGCGGACTC CTGTGACGGC AGATAATGAC AGTTTTCATG GGGGTGATAA TACACTTGCT CGCCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCTT
110 R A E D T A V Y Y C A K Y P H Y Y V N E R K S H W Y F D V W G Q G
^VH cys

2001 ACCTTGGTCA CGTCTCTCTC GGCCTCCACC AAGGGCCCAT CGGTCTTCCC CCTGGCACCC TCCTCCAAGA GCACCTCTTG GGGCACAGCG GCCCTGGGCT
TGGGACCACT GGCAGAGGAG CGGAGGTGG TTCCCGGTA GCCAGAAGG GACCCGTGG AGGAGTTCT CGTGAGACC CCCGTGTGCG CGGGACCCGA
143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C
Constant Heavy 1 (CH1) cys^

2101 GCCTGGTCAA GGACTACTTC CCGAACCGG TGACGGTCTC GTGGAATCA GCGGCCCTGA CCAGCGGGGT GCACACTTTC CCGGCTGTCC TACAGTCTCT
CGGACCACTT CTGATGAAG GGCCTTGGCC ACTGCCACAG CACCTTGAGT CGCGGGACT GGTGCGCA CGTGTGAAG GCGCGACAGG ATGTCAAGGAG
177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S
^CH1 cys

2201 AGGACTCTAC TCCTCAGCA GGTGTGTGAC TGTGCCCTCT AGCAGTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCAG CAACACCAAG
TCTTGAGATG AGGAGTCTG CGCACCACTG ACACGGGAGA TGTGCAACC CGTGGTCTG GATGTAGACG TTGCACCTAG TGTTCGGGTC GTTGTGGTTC
210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K
^CH1 cys

2301 GTGACACAAG AAGTTGAGCC CAAATCTTGT GACAAAATC ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTCAATC TTCCTCTTCC
CACCTGTTCT TTCAACTCGG GTTTAGAAC CTGTTTGG TGTGTAGCG TGGCACGGGT CGTGACTTG AGGACCCCC TGGCAGTCAG AAGGAGAGG
243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P
^cys to bind light chain ^hinge cys

2401 CCCCACCAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTACA TCGGTGGTGG TGGACGTGAG CCACGAAGAC CTGAGGTCA AGTTCAACTG
GGGGTTTTGG GTTCTGTGG GAGTACTAGA GGGCCTGGG ACTCCAGTGT ACGCACACC ACCTGCACTC GGTGCTTCTG GGACTCCAGT TCAAGTTGAC
277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W
^Constant Heavy 2 (CH2) cys

2501 GTACGTGAC GCGGTGGAGG TGCATAATGC CAAGACAAG CCGCGGAGG AGCAGTACA CAGCACGTAC CGTGTGTGTA CCGTCTCTAC CGTCTGAC
CATGCACCTG CCGCACCTCC AGTATTACG GTTCTGTTTC GGGCCCTCC TCGTCATGTT GTGCTGATG GCACACCACTG CGCAGGAGTG GCAGGACGTG
310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H
^CH2 cys

2601 CAGGACTGGC TGNATGGCAA GGAGTACAAG TGCAAGTCT CCAACAAGC CCTCCCAGCC CCCATCAGA AAACATCTC CAAAGCCAAA GGGCAGCCCC
GTCTGACCG ACTTACCGTT CCTCATGTT CAGTTCCAGA GGTGTTTCG GGAGGGTGG GGTAGTCTT TTGTGAGAG GTTTCGGTTT CCCGTGGGG
343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R
^CH2 cys

2701 GAGAACACA GGTGTACACC CTGCCCCCAT CCGGGAGA GATGACCAAG AACCAGTCA GCCTGACCTG CTGTGTCAAA GGCTTCTATC CCAGGACAT
CTCTTGGTGT CCACATGAG GACGGGGTA GGGCCCTTCT CTACTGTTCT TGTGTCAGT CCGACTGAC GGACCACTT CCGAAGATAG GGTTCGTGTA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I
^Constant Heavy 3 (CH3) cys

FIG. 18D

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2801 CGCGGTGGAG TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCTCCCGT GGTGGACTCC GACGGCTCCT TCTTCTCTA CAGCAAGCTC
CGGCACCTC ACCTCTCGT TACCCGTGG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTCGTTTCGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L
2901 ACCGTGGACA AGAGCAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGCAAGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTCGTCCAC CCGTGTCCG TTGCAGAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGATGTG CGTCTTCTCG GAGAGGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S
^CH3 cys
3001 CTCGGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTTG CGCGCGGGCG TTTTATTG TTAACATCATG TTTGACAGCT TATCATCGAT
GAGGCCCAT TATTCGTACG CTGCCGGAT CTCAGGGATT GCGAGCCAAC GCGGCGCCGC AAAAAATAAC AATTGAGTAC AAACGTGTGA ATAGTAGCTA
477 P G K O
^start lambda t0 terminator ^end lambda t0 terminator
^start of tet resistance promoter ^-35 of promoter
3101 AAGCTTTAAT GCGTAGTTT ATCACAGTTA AATTGCTAAC GCAGTCAGGC ACCGTGTATG AAATCTAACA ATGCGCTCAT GTCATCTC GGCACCGTCA
TTGGAATTA CGCATCAAA TAGTGTCAAT TTAACGATTG CGTCAGTCG TGGCACATAC TTAGATTGT TACCGAGTA GCAGTAGGAG CCGTGGCAGT
^-10 region of tet resistance promoter ^start of tet resistance translation
3201 CCCTGGATGC TGTAGGCATA GGCTTGTTA TGCCGGTACT GCGGGGCTC TTGCGGGATA TCGTCCATTC CGACAGCATC GCCAGTCACT ATGGCGTGCT
GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AAGCCCTAT AGCAGGTAAG GCTGTCGTAG CGGTCAGTGA TACCGCACGA
3301
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FIG. 19A

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1 GAATTCAACT TCTCCATACT ITGATAAGG AAATACAGAC ATGAAAAATC TCATTGTCTG GTTGTTATTT AAGCTTGCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTAG AGTAACGACT CAACAATAAA TTGGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GGCAGAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GAGCTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTGCG CAACTAACTA GTCCATCTCC

201 GGGCGCTGTA CGAGGTAAAG CCGATGCCA GCATTCTCTGA CGACGATACG GAGCTGTGTC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCACTA
CCCGGACAT GCTCCATTTT GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTCAGG GCGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTTGTAAGTA GTACGCCAAGT
TTTTCAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGGCTA CGTGTATATC
AGTGCATTTT TCCCATAGAT CTTAATACCTT CTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
Anti-VEGF Light chain (version Y0317)^
^STII Signal TIR -1

501 CAGTGTACCC AGTCCCGGAG CTCCTGTGTC GCCTGTGAG GCGATAGGT CACCATCAC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
GTCAACTGGG TCAGGGGCTC GAGGACACCG CGGTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCG GTTCTGGGAC
TAGTTGTCTT TGGTCTCTTT CGAGGCTTTC ATGACTAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGGTTGAA TAATGACAGT TGTCAATATCG TGGCAGCGCA CCTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTGCTTG ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTGCTCAACT TTAGACCTTG ACCAAGACAA CACACGGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCCGA GAGGCCAAG TACAGTGGAA GGTGATAC GCCTTCCAT CCGGTAATCT CAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K
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FIG. 19B

1001 GGACAGCACC TACAGCCTCA GCAGCACCTT GACGCTGAGC AAGCAGACT ACAGAAACA CAAAGTCTAC GCTGCGAAG TCACCCATCA GGCCTGAGC
CCTGCTGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTGT GTTTCAGATG CGACAGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAAAGAGCTT CAAACAGGGA GAGTGTTAAT TAAATCTCT AGCCCGGAGC CATCGTGGG AGTCGGTAC CCGGGATCT AGGCCTAACG
AGCGGCGAGT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGGAGA TGGGGCCCTG GTAGCACCGC TCAGACCATG GGCCTCTAGA TCGGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGT TTTTATTGTT GCGGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TCAATGCTT
GAGCCAACGG CGGCCGCAAA AAAATAACAA CGGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCACTG AGTTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGCTGTAC GAGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGTACGGTC GTAAAGGACTG CTGCTATGCC
1401 AGCTGCTGCG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCCTCAGTAA AAGTTAATC TTTCACACAG CTGTCAAAA GTTGTCACGG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCAAT TTTCATTTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGTCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTAAATGTAT TTGTAACCTAG TAGCCAAGTT CACGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCATTTT CCATAGATC TTAATATCTT TTCTTATAGC GTAAAGAAGA
1 M K K N I A F L L
^STII Signal TIR-1
1601 TGCACTATG TTGTTTTTT CTATTGCTAC AAACGGTAC GTCAGGTTC AGCTGGTCA GTCTGAGCA GAGTGAAAA AGCCAGGGC TTCAGTTAAA
ACGTAGATAC AAGCAAAAA GATACAGATG TTTCGCGATG CGAGTCCAAG TCGACCACTG CAGACCGGT CTCACCTTTT TCGTCCCGG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
^Anti-VEGF (version Y0317) Heavy Chain
^Heavy Chain FR1 changed to SubgroupI consensus sequence
1701 GTATCCTGTA AAGCTTCTGG CTACGACTTC AGCACTAGC GTATGAAGT GGTCCGTGAG GCCCGGGTA AGGCCCTGGA ATGGTTTGA TGGATTAACTA
CATAGGACAT TTGGAAGACC GATGCTGAAG TGGGTGATGC CATACTTGAC CCAGGCGATC CGGGGGCCAT TCCCGGACCT TACCCAACTT ACCTAATGT
43 V S C K A S G Y D F T H Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTATACCGG TGAACCGACC TATGCTGCGG ATTTCAAACG TCGTTTCACT TTTCCTTTAG ACACCTCAA AAGCACAGCA TACCTGCAGA TCAACAGCCT
GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAAAGAAATC TGTGAGGT TTCTGTGCTT ATGACCTCT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGGCTGAG GACACTGCGG TCTATTACTG TGCAAGTAC CGTACTATT ATGGAGGAG CCACTGTAT TTGACCTCTT GGGGTCAAGG AACCTGGTC
CGGCGACTC CTGTGACCGC AGATAATGAC AGTTTCTATG GGCATGATAA TACCCTGCTC GGTGACATA AAGTGCAGA CCCAGTTCC TTGGGACCAG
110 R A E D T A V Y Y C A K Y P Y Y Y G T S H W Y F D V W G Q G T L V
2001 ACCGTCTCT CCGCCTCCAC CAAGGGCCCA TGGTCTTCC CCGTGGCACC CTCCTCCAAG AGCACCTCTG GGGGCACAGC GGCCTTGGG TGCCTGGTCA
TGCAGAGGA GCGGAGGT GTTCCCGGT AGCAGAGG GGGACCGTGG GAGGAGTTC TCGTGGAGC CCGGAGTTCG CCGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 19C

2101 AGGACTACTT CCCGAACCG GTGACGGTGT CGTGAACATC AGGCGCCCTG ACCAGCGGG TGACACACCTT CCGGCTGTC CTACAGTCCT CAGGACTCTA
TCCTGATGAA GGGCTTGGC CACTGCCACA GCACCTTGAG TCCGCGGGAC TGGTCGCCGC ACGTGTGGAA GGGCGGACAG GATGTCAGAG GTCTTGAGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y
2201 CTCCTCAGC AGCGTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAG
GAGGAGTCG TCGCACCACT GACACGGGAG ATCGTCGAAC CCGTGGGTCT GGATGTAGAC GTTCACCTTA GTGTGCGGT CGTGTGGTT CCACCTGTTT
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K
2301 AAAGTTGAGC CCAATCTTG TGACAAACT CACACATGC CACCGTGCC AGCACCTGAA CTCCTGGGG GACGTCAGT CTTCTCTTTC CCCCCAAAC
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACGG GTGGCACGGG TCGTGGACTT GAGACCCCC CTGGCAGTCA GAAGGAGAAG GGGGTTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P
2401 CCAAGGACAC CCTCATGATC TCCCGGACCC CTGAGGTAC ATGCGTGGTG GTGACGTGA GCCACGAAGA CCTGAGGTC AAGTTCACT GGTAGGTGA
GGTTCTGTG GGAGTACTAG AGGCTTGGG GACTCCAGTG TACGCACCAC CACTGCACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACCT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D
2501 CGCGTGGAG GTGCATAATG CCAAGACAA GCCGCGGGAG GAGCAGTACA ACAGCACGTA CCGTGTGGTC AGCTCTCTCA CCGTCTTGA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTGTIT CGGCGCCCTC CTCGTCAAT GTGCTGCAAT GGACACCCAG TCGCAGGAGT GGCAGGACGT GGTCTTGACC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W
2601 CTGAATGGCA AGGAGTACAA GTGCAAGGTC TCCATCCAGC CCTCTCCAGC CCCATCGAG AAAACCATCT CCAAAGCCAA AGGCGAGCCC CGAGAACCAC
GACTTACCGT TCCTCATGTT CACGTCCAG AGGTGTTTC GGGAGGTCG GGGTAGCTC TTTTGGTAGA GGTTCGGTT TCCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q
2701 AGGTGTACAC CTTGCCCCCA TCCCGGGAAG AGATGACCAA GAACGAGTC AGCTGACCT GCCTGGTCAA AGGCTCTCTAT CCCAGCGACA TCGCCGTGGA
TCCACATGT GAGCGGGGT AGGCCCTTC TCTACTGGTT CTTGCTCCAG TCGACTGGA CGGACCACTT TCCGAAGATA GGTGCTGTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E
2801 GTGGGAGAGC AATGGGCAGC CGGAGAACA CTACAGACC AGCTCTCCG TGCTGGACTC CGACGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC
CACCTCTCG TTACCGTCG GCCTCTGTT GATGTTCTG GATGTTCTG TCGGAGGGC ACGACTGAG CTTGCCGAGG AAGAAGGAGA TGTGTTTGA GTGCACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D
2901 AAGAGCAGT GGCAGCAGG GAACGTCTTC TCATGCTCCG TGATGCATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTGCTCA CCGTGTCTCC CTTCAGAGAAG AGTACGAGC ACTACGTACT CCGAGACGTG TTGTGATGT CGGTCTTCTC GGAGAGGGAC AGAGCCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K
3001 AATAAGCATG CGACGCGCCT AGAGTCCCTA ACGTCTGGTT GCCGCGGGC GTTTTTATT GTTAACTCAT GTTTGACAGC TTATCATCGA TAAGCTTTAA
TTATTCGTAC GCTGCCGGGA TCTCAGGGAT TCGGAGCCAA CGGCGGCCCG CAAAAATAA CAATTGAGTA CAACTGTG AATAGTAGCT ATTGAAAT
477 O
3101 TCGGTAGT TATCAGATT AATTGCTAA CGCAGTCAGG CACCGTGTAT GAATCTAAC AATGCGTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG
ACGCCATCAA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGGCACATA CTTAGATTG TTACCGAGT AGCAGTAGGA GCCGTGGCAG TGGACCTAC

*Start Tet Resistance Coding Sequence

FIG. 19D

3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGGCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCCGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGTCACTG ATACCGCAGG ACGATCGCGA

3301

FIG. 20A

1 GAATTCAACT TCTCCATACT ITGGATAAGG AATACACAGAC ATGAAAAATC TCATTGTCTGA GTTGTATT TTTCGAAAGG AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTATGTCTG TACTTTTAG AGTAACGACT CAACAATAAA TTTCGAAAGG TTTTCTTCT TCTCAGCTTA
101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG AATTATCGTCA CTGCAATATG TCGCAAAATG GCGCAAAATG ACCAACACGG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CCGGTTTTAC TGGTGTGCG CAACATACTA GTCCATCTCC
201 GGGGCTGTGA CGAGGTAAG CCCGATGCCA GCATTCTCTGA CGACGATACG GAGTGTCTGC GCGATTACGT AAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCCGGACAT GCTCCATTTC GGGGTACGGT CGTAAGGACT GCTGCTATGC CTGACGACG CGCTAATGCA TTCTTCAAT AACTTCGTAG GAGCAGTCAT
301 AAAAGTTAAT CTTTCAACA GCTGTCAATA AGTTGTACG GCGAGACTT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT
TTTTCAAATTA GAAAGTTGT CGACAGTATT TCAACAGTGC CCGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AACATTGAT CATCGGTTCA
401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAGAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K N I A F L L A S M F V F S I A T N A Y A D I
^STII signal TIR-1 anti-IgE light chain^
501 CAGCTGACCC AGTCCCGAG CTCCTGTCC GCCTCTGTG GCGATAGGT CACATCAC TGCCGTGCCA GTCAGAGCGT CGATTACGAT GGTGATAGCT
GTCGACTGGG TCAGGGGCTC GAGGACACG CGGTATCCCA GTGTAGTGG ACGCACCGT CAGTCTCGCA GCTAATGCTA CCACTATCGA
26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y
601 ACATGAAC TGATCAACAG AACCCAGGAA AAGCTCCGAA ACTACTGATT TACCGGCGCT CGTACCTGGA GTCGTGAGTC CCTTCTCGCT TCTCTGGATC
TGTACTTGAC CATAGTTGTC TTTGGTCCCT TTGAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACCT CAGACCTCAG GGAAGAGCGA AGAGACCTAG
60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S
701 CGGTTCTGGG ACGGATTCA CTCGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAAGTC ACGAGGATCC GTACACATTT
GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTCGTCAGAC GTCGCCCTTC TGAAGCGTTG AATATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAA
93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F
801 GGACAGGTA CCAAGGTGA GATCAACGA ACTGTGGCTG CACCATCTGT CTTTCATCTC CCGCATCTG ATGAGCAGTT GAAATCTGGA ACTGCCTCTG
CCTGTCCCAT GGTTCACCT CTAGTTGCT TGACACCGAC GTGTAGACA GAAGTAGAAG GCGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC
126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V
901 TTGTGTCCCT GCTGAATAAC TTTATCCCA GAGAGGCCAA AGTACAGTGG AAGTGGATA ACGCCTCCA ATCGGTTAAC TCCAGGAGA GTGTACAGA
AACACACGGA CGACTTATTG AAGATAGGT CTCTCCGTT TCATGTCACC TTCCACCTAT TGCGGAGGT TAGCCCATTG AGGTCCTCT CACAGTGTCT
160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 20B

1101 GCAGGACAGC AAGACAGCA CCTACAGCCT CAGCAGCACC CTGACGCTGA GCAAGCAGA CTACGAGAAA CACAAAGTCT ACGCTGCGA AGTCAACCCAT
CGTCTGTGCG TTCCTGTGCT GGATGTGCGA GTCTGTGCTGG GACTGCGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TGGGACGCT TCAGTGGGTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H

1101 CAGGSCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCCGGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT
GTCCGGGACT CGAGCGGGCA GTGTTTCTCG AAGTTGTCC CTCTCACAAAT TAAATTAGGA GATCGGCCT GCCTAGCACC GCTCGAGCCA TGGGCCCTTA
226 Q G L S S P V T K S F N R G E C O

1201 CTAGSCCTAA CGCTCGGTTG CCGCCGGGCG TTTTATTG TTGCCGACGC GCATCTCGAA TGAATGTGT GCGCAGGTAG AAGCTTTGA GATTATCGTC
GATCCGGATT GCGAGCCAAC GCGGCCCGC AAAAATAAC AACGCTGG CGTAGAGCTT ACTTGACACA CCGTCCATC TTCGAAACCT CTAATAGCAG

1301 ACTGCAATGC TTCGCAATAT GCGCAAAAT GACCAACAGC GGTGTGTTGA TCAGGTAGAG GGGCGCTGT ACGAGGTAA GCGCATGCC AGCATTCCTG
TGACGTTACG AAGGTTATA CCGGTTTGA CTGGTTGTCG CCACTAACT AGTCCATCTC CCGCGGACA TGCTCCATTT CCGGCTACCG TCGTAAGGAC

1401 ACGAGCATAC GGAGTGTG CCGGATTACG TAAAGAAGTT ATTGAAGCAT CTTGTCAGT AAAAGTTAA TCTTTTCAAC AGCTGTCTATA AAGTTGTAC
TGCTGCTATG CCTCGACGAC GCGCTAATGC ATTCTTCAA TAACTTCGTA GGACAGTCA TTTTCAAAT AGAAAAGTTG TCGACAGTAT TTCAACAGTG

1501 GGCGGAGACT TATAGTCGCT TTGTTTTAT TTTTAAATGT ATTGTAACT AGTAGGCAAG TTCACGTAA AAGGTATCT AGAATTATGA AGAAGAATAT
CCGGCTCTGA ATATCAGCA AACAAAATA AAAAATTACA TAAACATTGA TCATGCGTTC AAGTCAATTT TTCCCATAGA TCTTAATACT TCTTCTTATA
M K K N I
^STII Signal TIR-1

1601 CGCAATTCCT CTTGATCTA GTTTCGTTTT TTCTATTGCT ACAACGCGT ACGTGAAGT TCAGCTGGTG GAGTCTGGG GTGGCCTGTT GCAGCCAGGG
GCGTAAAGAA GAACGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGGCA TGGACTCCA AGTCGACCAC CTCAGACCGC CACCGACCA CGTCGGTCCC
6 A F L L A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G
^anti-IgE heavy chain

1701 GGCTCACTCC GTTGTGCTG TGCAGTTTCT GGCTACTCCA TCACCTCCG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGTAAAGGC CTGGAATGGC
CCGAGTGAGG CAACAGGAC ACGTCAAGA CCGATGAGGT AGTGGAGGCC TATATCGACC TTGACCTAGG CAGTCCGGG CCCATTCCCG GACCTTACC
39 G S L R L S C A V S G Y S I T S G Y S W N W I R Q A P G K G L E W V

1801 TTGCATCGAT TACGTATGAC GGATCGACTA ACTATAACCC TAGCGTCAAG GGCGTATCA CTATAAGTCG CGACGACTCC AAAAACACAT TCTACCTGCA
AACGTAGCTA ATGCATACG CCTAGCTGAT TGATATTGG ATCCAGTTC CCGCATAGT GATATTACG GCTGCTGAGG TTTTGTGTA AGATGGACGT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q

1901 GATGAACAGC CTGCGTGTG AGGACACTGC CGCTATTAT TGTGTCGAG GCAGCCACTA TTTGCGTCA TGGCACTTCG CCGTGTGGG TCAAGGAACC
CTACTGTG GACGACGAC TCCTGTGACG GCAGATAA ACAGAGCTC CGTGGTGAT AAAGCAGTG ACCGTGAAGC GGCACACCCC AGTTCTTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W F A V W G Q G T

2001 CTGGTCACCG TCTCTCTGCG CTCACCAAG GGCCCATCG TCTTCCCCCT GGCACCCCTCC TCCAAGAGCA CCTCTGGGG CACAGCGGC CTGGGCTGCC
GACCAAGTGC AGAGAGCCG GAGGTGGTTC CCGGTAGCC AGAAGGGGA CCGTGGGAG AGGTCTCTCGT GGAGACCCCG GTGTCGCCCG GACCCGACCG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 20C

2101 TGGTCAAGGA CTACTTCCC GAACGGGTGA CGGTGTCGTG GAACTCAGGC GCCGTGACCA GCGCGGTGA CACTTCCCG GCTGTCCTAC AGTCTCAGG
ACCAATTCTT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCGG CCGGACTGTT CGCGCACCT GTGAAGGSC CGACAGGATG TCAGGAGTCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G

2201 ACTCTACTCC CTCAGCAGC TGGTGACTGT GCCCTCTAGC AGCTTGGGA CCGAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG
TGAGATGAGG GAGTCGTGCG ACCACTGACA CCGGAGATCG TCGAACCCGT GGTCTGGAT GTGACGTTG CACTTAGTGT TCGGTCGTT GTGTTCCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V

2301 GACAAAGAAAG TTGAGCCCAA ATCTGTGAC\AAACTCACA CATGCCACC GTGCCAGCA CTTGAACCTC TGGGGGACC GTGAGTCTTC CTCTTCCCCC
CTGTTCTTTC AACTCGGGTT TAGRACACTG TTTTGAGTGT GTACGGGTGG CACGGTCTGT GGACTGAGG ACCCCCTGG CAGTCAGAAG GAGAAGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P

2401 CAAACCCCAA GGACACCCTC ATGATCTCCC GGACCCCTGA GGTACATGC GTGTTGGTGG ACCTGAGCCA CGAAGACCCT GAGTCAAGT TCAACTGGTA
GTTTGGGTT CCTGTGGAG TACTAGAGG CCTGGGACT CCTGTAGC CACCACCAC TGCACCTGCT GTTCTGGGA CTCAGTTCA AGTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y

2501 GTGGACGGC GTGAGGTGC ATATGCCAA GACAAAGCG CCGGAGGAGC AGTAAACAG CAGTACCGT GTGTCAGCG TCCTACCGT CTGCACACG
GCACCTGCC CACCTCCACG TATTACGGTT CTGTTTCGGC GCCCTCTCG TCATGTTGTC GTGCATGGCA CACCACTCGC AGGAGTGGCA GGAGTGTGTC
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q

2601 GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGTCTCCA ACAAGCCCT CCAGCCCCC ATCAGAAARA CCATCTCCA AGCCAAAGG CAGCCCCGAG
CTGACCGACT TACGTTCTCT CATGTTACG TTCCAGAGT TGTTTCGGA GGTCGGGG TAGTCTTTT GTGAGAGTT TCGTTTCCG GTCGGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E

2701 AACCACAGGT GTACACCCTG CCCCATCCC GGGAAAGAGT GACCAAGAAC CAGTACAGC TGACCTGCCT GGTCAAAGGC TTCTATCCA GCGACATCGC
TTGGTGTCCA CATGTGGAC GGGGGTAGG CCTTCTCTA CTGTTCTTG GTCCAGTCGG ACTGGACGA CCAGTTTCCG AAGATAGGT CGCTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A

2801 CGTGGAGTG GAGACCAATG GGCAGCCGA GAACAACATC AAGACCACG CTCCTCGTGT GGACTCCGAC GGCTCTTCT TCCTCTACAG CAAGCTCACC
GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTCTGTATG TTCTGGTGG GAGGCGACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T

2901 GTGGACAAGA GCAGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGT CTGCACAAAC ACTACACGA GAAGAGCCTC TCCTGTCTC
CACCTGTTCT CGTCACCGT CGTCCCTTG CAGAAGATG CAGGCACCTA CGTACTCGA GAGTGTGG TGATGTGCT CTCTCGGAG AGGACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P

3001 CCGGTAATA AGCATGCGAC GGCCTAGAG TCCCTAACG TCGTTGCCG CCGGGCGTT TTTATGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGATTTGCG AGCCAACGGC GGCCCGCAA AATAACAAT TGAGTACAAA CTGTGGAATA GTAGCTATT
473 G K O

3101 CTTTAATGCG GTAGTTTATC ACAGTTAAAT TGCTAACGCA GTACGGCACC GTGTATGAA TCTAACAAAT CGCTCATCGT CATCTCGGC ACCGTACACC
GAATACCG CATCAATAG TGTCAATTTA ACGATTGCGT CAGTCCGTG CACATCTTT AGATTGTTAC GCGAGTAGCA GTAGGAGCGG TGGCAGTGGG

FIG. 20D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCTCTTG CGGATATCG TCCATTCCGA CAGCATCGCC AGTCACTATG GCGTGCTGCT
ACCTAGGACA TCCGTATCCG AACCAATACG GCCATGACGG CCCGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGGACGA
3301

FIG. 21A

1 GAATTCAACT TCCTCATACT TTGGATAAGG AAATACAGAC ATGAAATAATC TCATTGCTGA GTTGTATT TT AACCTTGCC AAAAAGAAGA AGAGTCGAAT
CITTAAGTTGA AGAGGTATGA AACCTATTCC TTATATGCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTGGAACGGG TTTTTCCTCT TCTCAGCTTA
101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTCGAATGCT TCGCAATATG CGCAAAATG ACCAAACAGCG GTTGATTGAT CAGGTAGAGG
CITGACACAC GCGTCCATCT TCGAAACCTC TAATAGCACT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTGTGCG CAACTAAC TA GTCCATCTCC
201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCCTGA CGAGCATAGG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTGCTCAGTA
CCGCGGACAT GCTCCATTTC GGGCTACGCT CGTAAGGACT GCTGCTATGC CTCGACGAGG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT
301 AAAAGTTAAT CTTTCAACA GCTGTCATAA AGTTGTCAG GCCGAGACTT ATAGTCGCTT TGTTTTTTATT TTTTAATGTA TTTGTAAC TA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTAAT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA
401 TCACGTAAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCTA CGCTGATATC
AGTGCAATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^StII signal TIR-1 anti-IgE light chain^
501 CAGCTGACCC AGTCCCCGAG CTCCTGTCC GCCTCTGTGG GCGATAGGCT CACCATCACC TGCCGTGCCA GTCAGAGCGT CGATTACGAT GGTGATAGCT
GTCGACTGGG TCAGGGGCTC GAGGACACAG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGGCACGCT CAGTCTCGCA GCTAATGCTA CCACTATCGA
26 Q L T Q S P S S L S A S V G D R V T I T C R A S Q S V D Y D G D S Y
601 ACATGAAC TGATCAACAG AAACCAAGAA AAGTCCGAA ACTACTGATT TACGCGGCTT CCGTACCTGA GTCTGGAGTC CCTTCTCGCT TCTCTGGATC
TGTTACTTGAC CATAGTTGTC TTGGTCCCTT TTGAGGCTT TGATGACTAA ATGCGCCGGA GCATGGACT CAGACCTCAG GGAAGAGCGA AGAGACCTAG
60 M N W Y Q Q K P G K A P K L L I Y A A S Y L E S G V P S R F S G S
701 CGGTTCTGGG ACGGATTTCA CTCGACCAT CAGCAGTCTG CAGCCGGAAG ACTTCGCAAC TTATTACTGT CAGCAAGTC ACGAGGATCC GTACACATTT
GCCAAGACCC TGCCTAAAGT GAGACTGGTA GTGCTCAGAC GTGCGCTTC TGAAGCGTTG AATAATGACA GTCGTTTCAG TGCTCCTAGG CATGTGTAAA
93 G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q S H E D P Y T F
801 GGACAGGGTA CCAAGGTGA GATCAAAACGA ACTGTGGCTG CACCATCTGT CTTCACTTTC CCGCATCTG ATGAGCAGTT GAAATCTGA ACTGCCCTCG
CCTGTCCCAT GGTTCACCT CTAGTTTGTG TGACACCGAC GTGGTAGACA GAAGTAGAAG GCGGGTAGAC TACTCGTCAA CTTTAGACCT TGACGGAGAC
126 G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V
901 TTGTGTGCCT GCTGAATAC TTCTATCCCA GAGAGGCCAA AGTACAGTGG AAGTGGATA ACGCCCTCCA ATCGGGTAAC TCCAGGAGA GTGTCACAGA
AACACACGGA CGACTTAITG AAGATAGGCT CTCTCCGGTT TCATGTCACC TTCCACCTAT TGGGGGAGT TAGCCCAITG AGGTCTCTCT CACAGTGTCT
160 V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E

FIG. 21B

1101 GCAGGACAGC AAGACAGCA CCTACAGCCT CAGCAGCACC CTGACGCTGA GCAAGAGAGA CTACGAGAAA CACAAAGTCT ACGCCTGCGA AGTCACCCAT
CGTCTGTCTG TTCTGTCTGT GGATGTGCGA GTCTGCTGTG GACTGCGACT CGTTTCGTCT GATGCTCTTT GTGTTTCAGA TCGCGACGCT TCAGTGGGTA
193 Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H
1101 CAGGGCCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG GAGAGTGTTA ATTAAATCCT CTACGCCGA CGCATCGTGG CGAGCTCGGT ACCCGGGGAT
GTCCCGGACT CGAGCGGCA GTGTTTCTCG AAGTGTGCC CTCTCACAAAT TAATTTAGGA GATCGGCGCT GCGTAGCACC GCTCGAGCCA TGGGCCCCCTA
226 Q G L S S P V T K S F N R G E C O
1201 CTAGGCCCTAA CGCTCGGTTG CGCCCGGGCG TTTTATTATG TTGCCGAGCG GCATCTCGAA TGAATCTGTG GCGCAGGTAG AAGCTTTTGA GATTATCTGC
GATCCGGATT GCGAGCCAAAC GCGGCCCCGC AAAAATAAAC AACGGCTGCG CGTAGAGCTT ACTTGACACA CCGCTCCATC TTGGAACCT CTAATAGCAG
1301 ACTGCAATGC TTCGCAATAT GCGCAAAAT GACCAACAGC GGTGTGATTGA TCAGGTAGAG GGGGCGCTGT ACAGAGTAAA GCCCGATGCC AGCATTCCTG
TGAGTTACG AAGGTTTATA CCGGTTTATA CTGGTTGTG CCAACTAAT AGTCCATCTC CCCC CGGACA TGCTCCAATT CCGGCTACGG TCGTAAGGAC
1401 ACGACGATAC GGAGCTGCTG CCGGATTACG TAAAGAAATT ATTGAAGCAT CCTCGTCACT AAAAAGTTAA TCTTTTCAAC AGCTGTCTATA AAGTTGTAC
TGCTGTATG CCTCGACGAC GCGCTAATGC ATTCTTTCAA TAACTTCGTA GGAGCAGTCA TTTTTCAAAT AGAAAAGTTG TCGACAGTAT TTCAACACAGT
1501 GCGCGAGACT TATAGTCGCT TTGTTTTTAT TTTTAAATGT ATTTGTAAT AGTACGCAAG TTCACGTTAA AAGGTAATCT AGAATTATGA ABAAGAAAT
CCGCTCTGA ATATCAGCGA AAAAAAATA TAAACATTGA TCATCGCTTC AAGTCAATT TTCCCATAGA TCTTAATACT TCTTCTTATA
M K K N I
1
^STII Signal TIR-1
1601 CGCATTTCTT CTTCATCTA TGTTCTGTTT TTCTATTGCT ACAAGCGGT ACGTCAAGT TCAGCTGCNA GAGTCTGGC CGGGCCTGGT GAAACCACT
GCGTAAAGAA GAAGTAGAT ACAAGCAAAA AAGATAACGA TGTTTGCGA TGCAGTCCA AGTCAGCTT CTGAGACCG GCGCGGACCA CTTTGGTGA
6 A F L L A S M F V F S I A T N A Y A Q V Q L Q E S G P G L V K P S
^anti-IgE Heavy Chain
^Heavy Chain FR1=SubgroupII consensus sequence
1701 CAGACTCTCT CTTGACTTG TACTGTTTCT GGCTACTCCA TCACCTCCG ATATAGCTGG AACTGGATCC GTCAGGCCCC GGGTAAAGGC CTGGAATGG
GTCTGAGAGA GGAATGAC ATGACAAAGA CCGATGAGT AGTGAGGCG TATATCGACC TTGACCTAGG CAGTCCGGG CCCATTCCG GACCTTACCC
39 Q T L S L T C T V S G Y S I T S G Y S W N W I R Q A P G K G L E W V
1801 TTGCATCGAT TACGATGAC GATCGACTA ACTATAACC TAGGTCGAAG GGCGTATCA CTATAAGTGC CGACGACTCC AAAAACACAT TCTACCTGCA
AACGTAGCTA ATGCATACG CCTAGCTGAT TGATATTGG ATCGAGTTT CCGCATAGT GATATTACG GCTGCTGAGG TTTTGTGTA AGATGGAGCT
73 A S I T Y D G S T N Y N P S V K G R I T I S R D D S K N T F Y L Q
1901 GATGAACAGC CTGCGTGTG AGGACACTGC CGTCTATTAT TGTCCTGAG GCAGCCACTA TTTTCGTCAC TGGCACTTCG CCGTGTGGG TCAAGGAACC
CTACTGTG GACGACGAC TCCTGTGACG GCAGATAATA ACACGAGCTC CGTCGGTAT AAGCCAGT AAGCCAGT ACCGTGAAG GGCACACCCC AGTTCCTTGG
106 M N S L R A E D T A V Y Y C A R G S H Y F G H W F A V W G Q G T
2001 CTGCTCACCG TCTCTCGGC CTCACCAAG GGCCCATCG TCTTCCCCCT GGCAACCTCC TCCAAGAGCA CTTCTGGGG CACAGCGGC CTGGGCTGCC
GACCAGTGGC AGAGAGCCG GAGGTGTTT CCGGTAGCC AGAAGGGGA CCGTGGGAGG AGGTCTCTGT GGAGACCCC GTGTGCGCGG GACCCGACCG
139 L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L

FIG. 21C

2101 TGGTCAAGGA CTACTTCCCG GAACCGGTGA CGGTCTCGTG GAACCTCAGG GCCCTGACCA GCGGGGTGCA CACCTTCCCG GCTGTCCTAC AGTCCTCAGG
ACCACTTCCT GATGAAGGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGGT CGCGCACGT GTGGAAGGCG CGACAGGATG TCAGGAGTCC
173 V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G

2201 ACTCTACTCC CTCAGCAGCG TGGTGACTGT GCCCTTAGC AGTTGGGCA CCACAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCAA CACCAAGGTG
TGAGATGAGG GAGTCGTGCG ACCACTGACA CGGAGATCG TCGAACCCGT GGGTCTGGAT GTAGACGTG CACTTAGTGT TCGGGTCTGT GTGGTTCCAC
206 L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V

2301 GACAAGAAAG TTGAGCCCAA ATCTTGTGAC¹ ABAACTCACA CATGCCACC GTGCCAGCA CCTGAACCTC TGGGGGGACC GTCACTCTTC CTCTTCCCCC
CTGTTCTTTC AACTCGGGTT TAGAACACTG TTTTGAGTGT GTACGGGTGG CACGGTCTGT GGACTTAGG ACCCCCCTGG CAGTCAGAAG GAGAAGGGGG
239 D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P

2401 CAAAACCCAA GGACACCCCTC ATGATCTCC GGACCCCTGA GGTCACTAGC GTGTGGTGG ACCTGAGCCA CGAAGACCTT GAGTCAAGT TCAACTGTGA
GTTTGGGTT CCTGTGGGAG TACTAGAGG CCTGGGACT CAGTGTAGC CACCACCACC TGCACCTGGT GCTTCTGGGA CTCACGTTCA AGTTGACCAT
273 K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y

2501 CGTGGACGGC GTGGAGGTGC ATATGCCCCA GACAAAGCCG CGGAGGAGC AGTACAACAG CAGTACCGT GTGGTCAGG TCCTCACCGT CCTGCACACG
GCACCTGCCG CACCTCCACG TATTACGGTT CTGTTTCGGC GCCCTCCTCG TCATGTTGTC GTGCATGGCA CACCAGTGC AGGAGTGGCA GGACGTGCTC
306 V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q

2601 GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGTCTCCA ACAAGCCCT CCAGCCCCC ATCGAGAAAA CCATCTCAA AGCAAAGGG CAGCCCCGAG
CTGACCGACT TACCGTTCCT CATGTTACG TTCCAGAGT TGTTTCGGA GGTTCGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC GTCGGGGCTC
339 D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E

2701 AACCAACAGT GTACACCCCTG CCCCCATCC GGAAGAGAT GACCAAGAAC CAGGTCAGC TGACCTGCTT GGTCAAAGGC TTCTATCCCA GGCACATCGC
TTGGTGCCA CATGTGGGAC GGGGTAGG CCTTCTCTA CTGTTCTTG GTCCAGTCCG ACTGGACCGA CCAGTTTCCG AAGATAGGTT CGCTGTAGCG
373 P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A

2801 CGTGGAGTG GAGAGCAATG GGCAGCCGGA GAACAACACTA AAGACCAAGC CTCCTGCTGT GGACTCCGAC GGCTCTTCT TCCTCTACAG CAAGCTCACC
GCACCTCACC CTCTCGTTAC CCGTCGGCTT CTGTTGATG TTCTGGTGG GAGGGCAGCA CTGAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG
406 V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T

2901 GTGACACA GAAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGCT CTGCACAACC ACTACACGCA GAAGAGCCTC TCCCTGTCTC
CACCTGTTCT CGTCCACCGT CGTCCCCCTG CAGAAGAGTA CGAGGCACTA CGTACTCGA GAGGTGTGG TGATGTGGT CTCTCTCGAG AGGACAGAG
439 V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P

3001 CGGGTAAATA AGCATGCCAC GGCCCTAGAG TCCTAAAGC TCGGTTGCG CGGGCGGTTT TTTATGTTA ACTCATGTTT GACAGCTTAT CATCGATAAG
GCCCATTTAT TCGTACGCTG CCGGATCTC AGGGATTGG AGCCAACGGC GGCCCCGAAA AAATAACAAT TGAGTACAAA CTGTGGAATA GTAGCTATTCT
473 G K O

3101 CTTTAATGG GTAGTTTATC ACAGTTAAAT TGTAACGCA GTACAGGACC GTGTATGAAA TCTAACATG CGCTCATGCT CATCTCGGC ACCGTCAACC
GAAATTACG CATCAATAG TGTCAATTTA ACAGTTGCT CAGTCCGTTG CACATCTTT AGATTGTTAC GCGAGTAGCA GTAGGAGCCG TGGCAGTGGG

FIG. 21D

3201 TGGATGCTGT AGGCATAGGC TTGGTTATGC CGGTACTGCC GGGCCTCTTG CCGGATATCG TCCATTCCGA CAGCATCGCC AGTCACTATG GCCTGCTGCT
ACCTACGACA TCCGTATCCG AACCAATACG GCCATGACCG CCCGGAGAAC GCCCTATAGC AGGTAAGGCT GTCGTAGCGG TCAGTGATAC CGCAGGACGA

3301

FIG. 22A

1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACACAGC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

101 GAACGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCTCA CTGCAATGCT TCGCAATPAT GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGGTTTAC TGGTTGTCGC CAACTAAC TA GTCCAATCTCC

201 GGGCGCTGA CGAGGTAAAG CCGATGCCA GCATTCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTACGTA
CCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGAGC CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

301 AAAAGTTAAT CTTTTCACA GCTGTCAFAA AGTGTCAAG GCGGAGACTT ATAGTCGCTT TGTTTTATTT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

401 TCACGTAAA AGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTCGCAT GCGACTATAG

1 M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1 anti-VEGF Light Chain (1st generation)^

501 CAGATGACCC AGTCCCCGAG CTCCTGTTC GCCTGTGG GCGATAGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT
GTCTACTGGG TCAGGGGCTC GAGGACAGG CGGTATCCCA GTGGTAGTGG AGCTCGCGTT CAGTCCCTATA ATCGTTGATA AATTGACCA

26 Q M T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTTA CTTACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGATCCG GTTCTGGAC
TAGTTGTCTT TGGTCCITTT CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTG

60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G S G T

701 GGATTTCACT CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCGGT GGACGTTGG ACAGGTTACC
CCTAAAGTGA GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCAATCG TGGCACGSCA CCTGCAAAACC TGTCCCATGG

93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

801 AAGTGGAGA TCAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGTCTCTGTT GTGTGCTGC
TTCCACCTCT AGTTTGTCTG ACACCGACGT GGTAGACAGA AGTAGAAGG CGGTAGACTA CTCGTCACT TTAGACCTTG ACGAAGACAA CACACGACG

126 K V E I K R T V A A P S V F I F P P S D E Q L K S G T A S V V C L L

901 TGAATAACTT CTATCCAGA GAGGCCAAAAG TACAGTGGAA GGTGGATAAC GCCTCCCAAT CCGGTAATCT CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACCTT CCACCTATTG CCGGAGGTTA GCCCATTCAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGTT

160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

FIG. 22B

1001 GGACAGCACC TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAACAGAGCT ACAGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCCTGAGC
CCTGCTGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTCAGATG CGACGCTTC AGTGGGTAGT CCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S
1101 TCGCCCGTCA CAACAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGAGC CATCTGTGGG AGCTCGGTAC CCGGGGATCT AGGCCTAAGC
AGCGGGCAGT GTTCTCGAA GTTGTCCCT CTCAAAATTA ATTTAGGAGA TCGGGCCTGC GTAGCACCGC TCAGACCATG GGGCCCTAGA TCCGGATTGC
226 S P V T K S F N R G E C O
1201 CTCGGTTGCC GCGGGCGT TTTTATTGTT GCCGACGGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCATATGCTT
GAGCCAACGG CCGCCCGCAA AAAATAACAA CCGCTGCGG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTACGAA
1301 CGCAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGGG GCGCTGTAC GAGGTAAAG CCGATGCCAG CATTCCTGAC GACGATACGG
GCGTTATACC GCGTTTACT GGTGTGCGC AACTAACTAG TCCATCTCCC CCGCGACATG CTCATTTCC GGTACGGTC GTAAGGACTG CTGCTATGCC
1401 AGTCTCTGCG CGATTACGTA AAGAGTTAT TGAAGCATCC TCGTCAGTAA AAGTTAATC TTTTCAACAG CTGTCATAAA GTTGTACCG CCGAGACTTA
TCGACGACGC GCTAATGCAI TTCTTCAATA ACTTCGTAG AGCAGTCAIT TTTCAAITAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT
1501 TAGTCGCTTT GTTTTATTT TTTAATGTAT TTGTAAC TAGCCAAGTT CACGTAAAAA GCGTATCTAG AATTATGAAG AAGAATATCG CATTTCTTCT
ATCAGCGAAA CAAAAATAA AAATTACATA AACATTGATC ATGCGTTCAA GTGCAITTTT CCCATAGATC TTCTTATAGC GTAAAGAAAGA
1 M K K N I A F L L
1 ^STII Signal TIR-1
1601 TGCATCTATG TTCTTTT TTTTCTTCTAC AAACGCGTAC GCTGAGTTTC AGCTGGTGA GTCTGGCGGT GGCCTGTGTC AGCCAGGGG CTCACCTCCGT
ACGTAGATAC AAGCAAAAAA GATAACGATG TTTCGCGATG CGACTCCAAG TCGACCACTT CAGACCGCA CCGGACCCAG TCGTCCCCC GAGTGAGCA
10 A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R
^anti-VEGF (1st generation) heavy chain
1701 TTGTCCTGTG CAGCTTCTGG CTATACCTTC ACCAATATG GTATGAATG GTTCCGTGAG GCGCCGGGTA AGGGCTTGA ATGGTTTGA TGGATTACA
AACAGGACAC GTCGAAGACC GATATGAAG TGGTTGATAC CATACTGAC CCAGGCAGTC CCGGGCCCAT TCCGGGACCT TACCCAACT ACCTAAITGT
43 L S C A A S G Y T F T N Y G M N W V R Q A P G K G L E W V G W I N T
1801 CCTAPACCGG TGAACCGACC TATGCTGCGG AITTCAAAAG TCGTTTCACT TTCAAGCTTAG ACACCTCCAA GTGACACAGA TACCTGCAGA TGAACAGCCT
GGATATGCC ACTTGGCTGG ATACGACGCC TAAAGTTTGC AGCAAGTGA AAGTCGAATC TGTGGAGTTT CAGCTGTGCT ATGACAGTCT ACTTGTGCGA
77 Y T G E P T Y A A D F K R R F T F S L D T S K S T A Y L Q M N S L
1901 GCGTGTGAG GACACTGCCG TCTATTACTG TGCAAGTAC CCCCCTATT ATGGGAGCAG CCACTGGTAT TTGACGCTT GGGGTCAAGG AACCTGTGTC
CGCAGGACTC CTGTGACGGC AGATAATGAC ACGTTTCTAG GGGGTGATAA TACCTCTGTC GGTGACCATTA AAGTGCAGA CCCAGTTCC TTGGGACGAG
110 R A E D T A V Y Y C A K Y P H Y Y G S S H W Y F D V W G Q G T L V
2001 ACCGTCTCT CGGCTCCAC CAAGGGCCCA TCGTCTTCC CCGTGGCACC CTGCTCCAAG AGCACCTCTG GGGGCACAGC GGCCTGGGC TGCCTGGTCA
TGGCAGAGGA GCGGAGGTG GTTCCCGGGT AGCCAGAAGG GGGACCGTGG GAGGAGTTTC TCGTGGAGC CCGGTGTG CCGGACCCG ACGGACCACT
143 T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C L V K

FIG. 22C

2101 AGGACTACTT CCCCAGACCG GTGACGGTGT CGTGGAACTC AGCGGCCCTG ACCAGCGGGG TGCACACCTT CCGGCTGTC CTACAGTCTT CAGGACTCTA
TCCTGATGAA GGGCTTGGC CACTGCCACA GCACCTTAGT TCGCGGGAC TGCTGCCGC ACCTGTGGA ACCTGTGGA GATGTACGAG GTCTGAGAT
177 D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S G L Y

2201 CTCCTCAGC AGCTGGTGA CTGTGCCCTC TAGCAGCTTG GGCACCCAGA CTFACATCTG CAAAGTGAAT CACAAGCCCA GCAACACCAA GGTGGACAAAG
GAGGAGTGC TCGCACCACT GACACGGGAG ATGTCTGAAC CCGTGGGTCT GGATGTAGAC GTTGACACTTA GTTGTGGGT CGTTGTGGTT CCACCTGTTT
210 S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K V D K

2301 AAAGTTGAGC CCAATCTTG TGACAATACT CACATATGCC CACCGTGCC AGCACCTGAA CTCCTGGGG GACCGTCAGT CTTCTCTCTC CCCCCAAAAC
TTTCAACTCG GGTTAGAAC ACTGTTTGA GTGTGTACG GTGCACGGG TCGTGACCTT GAGGACCCCT CTGCGAGTCA GAAGGAGAG GGGGGTTTTG
243 K V E P K S C D K T H T C P P C P A P E L L G G P S V F L F P P K P

2401 CCAAGGACAC CCTCATGATC TCCGGACCC CTGAGGTAC CATTGGTGGT GTGGACGTGA GCCACGAAGA CCTGAGGTC AGTTCAACT GGTACGTGGA
GGTTCTCTGT GGAGTACTAG AGGSCCTGG GACTCCAGT TACGCACCA CACTGCACT CGGTGCTTCT GGGACTCCAG TTCAAGTTGA CCATGCACTT
277 K D T L M I S R T P E V T C V V V D V S H E D P E V K F N W Y V D

2501 CGCGTGGAG GTGCATAATG CCAAGACAAA GCCCGGGAG GAGCAGTACA ACAGCACGTA CCGTGTGGT AGCGTCTCTCA CCGTCTCTCA CCAGGACTGG
GCCGACCTC CACGTATTAC GGTCTGTGTT CGCGCCCTC CTGCTCATGT TGTGTGAT TGCACACCA GGCACAGGAGT TCGCAGGAGT GGTCTCTGAC
310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W

2601 CTGAATGGCA AGGAGTACAA GTGCAAGTTC TCCAACAAAG CCTCTCCAGC CCCATCTGAG AAAACCATCT CCAAAGCCAA AGGCGAGCC CGAGAACCAC
GACTTACCGT TCCTCATGTT CAGTTCCAG AGTTGTTTC GGGAGGTCG GGGTAGCTC TTTTGGTAGA GGTTCGGT TCCCGTCGG GCTCTTGGT
343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q

2701 AGGTGTACAC CTTGCCCCCA TCCCGGGAAG AGATGACCAA GAACAGGTC AGCTGACCT GCCTGGTCAA AGGCTTCTAT CCCAGCGACA TCGCCGTGGA
TCCACATGT GAGCGGGGT AGGCCCTTC TCTACTGTT CTGTGTCCAG TCGACTGGA CGGACCACTT TCCGAAGATA GGTCTGCTGT AGCGCACCT
377 V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I A V E

2801 GTGGAGAGC AATGGGCAGC CGGAGAACAA CTACAAGACC ACGCTCCCG TGTGGACTC CGAGGGCTCC TTCTTCTCT ACAGCAAGCT CACCGTGGAC
CACCTCTCG TTACCGTGC GCCTCTTGT GATGTTCTGG TCGGAGGGC ACGACCTGAG GCTGCCGAGG AAGAAGGAGA TGTGTTTCA GTGCGACCTG
410 W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L T V D

2901 AAGACAGGT GGCAGCAGG GAAGTCTTC TCATGCTCCG TGATGCATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGTA
TTCTGTTCA CCGTGTGCC CTTGCAGAG AGTACGAGG ACTACGTACT CCGAGACGTG TTGTGATGT GCGTCTTCTC GGAGAGGGAC AGAGGCCCAT
443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S L S P G K

3001 AATAAGCATG CGAGGCCCTT AGAGTCCCTA ACGTCTGGTT GCCCGCGGC GTTTTTTATT GTTAACTCAT GTTTGACAGC TTATCATGA TAAGCTTTAA
TTATTCTGAC GCTGCCGGA TCTCAGGGAT TCGAGGCCAA CGCGCGCCCG CAAAANATTA CAATTGAGTA CAACTGTCTG AATAGTAGCT ATTGGAATTT
477 O

3101 TCGGTAGTAT TATCAGATT AATTTGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC AATGCGTCA TCGTCATCTT CGGCACCGTC ACCCTGGATG
ACGCCATCAA ATAGTGTCAA TTTAACGATT GCGTCAGTCC GTGCACATA CTTTAGATTG TTACGCGAGT AGCAGTAGGA GCCGTGGCAG TGGACCTAC

3201 CTGTAGGCAT AGGCTTGGTT ATGCGGTAC TGCCGGGCTT CTTGCGGAT ATCGTCCATT CCGACAGCAT CGCAGTCAAC TATGGCGTGC TGCTAGCGCT
GACATCCGTA TCCGAACCAA TACGCCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTCTGA GCGTCAAGT ATACCGCAGG ACATCGCA

FIG. 23A

>Anti-VSGF (VNERK version) IgG1 Expression Cassette with heavy chain FR1,2,3,4=consensus subgroup I

ecorI pflMI bsrDI hindIII earI/ksp6321
1 GAATTCAACT TCTCCATACCT TTGGATAAGG AATACAGAC ATGAAAATC TCATTGCTGA GTTGTATTAT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGCTG TACTTTTATG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTCTTCT TCTCAGCTTA

bspMI bsrDI bclI
101 GAACTGTG CCGAGGTAGA AGCTTGGAG ATTATCTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CCGGTTTTAC TGGTTGTGCG CAACCTAATA GTCCATCTCC

bsmI snaBI
201 GGGCGCTGA CAGAGTAAAG CCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTGAGTA
CCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

ahdI/eam1105I speI
301 AAAAGTTAAT CTTTCAACA GCTGTGATAA AGTGTGACG GCCGAGACT ATAGTCGCTT TGTTTTATT TTTTAATGTA TTGTAACTA GTACGCAAGT
TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AACATTGAT CATGCGTTCA

pvuII eagI/xmaIII/ec1XI
401 TCACGTAAA AGGTATCTA GAATTATGA GAAGATATC GCATTCTTC TTGCATCTAT GTTCGTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC
AGTGCATTTT TCCCATAGAT CTTAATACTT CTCTTATAG CGTAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG
M K K N I A F L L A S M F V F S I A T N A Y A D I
^STII Signal TIR -1

xbal bsiWI/splI mluI ecorV
501 CAGTTGACCC AGTCCCGAG CTCCCTGTC GCTCTGTGG GCGATAGGT CACCATCACC TGCAGGCAA GTCAGGATAT TAGCAACTAT TAAACTGGT
GTCAACTGGG TCAGGGCTC GAGGACAGG CCGAGACACC CGCTATCCCA GTGTAGTGG ACCTGCGTT CAGTCTATA ATCGTTGATA AATTGACCA
26 Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y

estI pstI
601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTGTCTT TGGTCTTTT CGAGGCTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

bsaI bspMI bseRI bpmI/gsuI bamHI
601 ATCAACAGAA ACCAGGAAA GCTCCGAAG TACTGATTA CTTACCTCC TCTCTCCACT CTGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC
TAGTGTCTT TGGTCTTTT CGAGGCTTC ATGACTAAAT GAAGTGGAG AGAGAGGTGA GACCTCAGG AAGAGCGAAG AGACCTAGG CAAGACCTG
60 Q Q K P G K A P K V L I Y F T S S L H S G V P S R F S G S G T

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kpnI      asp718      acc65I
701 GGATTTCAC TCGACCATCA GCAGTCTGCA GCCAGAGAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT GGACGTTTGG ACAGGGTTACC
CCTAAAGTGA GACTGGTAGT CGTCAGAGCT CGGTCTCTCG AAGCGTTGAA TAATGACAGT TGTATATATCG TGGCAGCGCA CCTGCAAAACC TGTCCCATGG
93 D F T L T I S S L Q P E D F A T Y Y C Q Q Y S T V P W T F G Q G T

xmniI      bpuAI      bbsI
801 AAGGTGGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCCTGC
TTCCACCTCT AGTTTGTCTG ACACCGAGCT GGTAGACAGA AGTAGAAGG I F P P S D E Q L K S G A S V V C L L
126 K V E I K R T V A A P S V F I F P P S D E Q L K S G A S V V C L L

xmniI      asp700
901 TGAATAACTT CTATCCGAGA GAGGCCAAG TACAGTGGAA GGTGATAAC GCCTCCAAT CGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA
ACTTATTGAA GATAGGTCT CTCGGTTC ATGTACCTT CCACCTATTG CGGAGGTTA GCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT
160 N N F Y P R E A K V Q W K V D N A L Q S G N S Q E S V T E Q D S K

cellI/espI      blpI/bpul102I
1001 GACAGACACC TACAGCTCA GACGCTGAGC AAGCAGACT ACAGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA GGGCTCTGAGC
CCTGTCTGG ATGTGAGT CGTGTGGGA CTGCGACTCG TTCTGTCTGA TGCTCTTGT GTTTCAGATG CGGACGCTTC AGTGGTAGT CCCGGACTCG
193 D S T Y S L S S T L T L S K A D Y E K H K V Y A C E V T H Q G L S

xmaI/pspAI
1101 TCGCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTAAAT TAAATCCTCT ACGCCGAGC CATCGTGCG AGCTCGGTAC CCGGGATCT AGGCTTAACG
AGCGGAGCT GTTCTCGAA GTTGTCCCT CTCACAATTA ATTAGGAGA TGCGGCTGC GTAGACCCG TCGAGCCATG GGCCCTAGA TCCGATTGC
226 S P V T K S F N R G E C O

start lambda t0 terminator

bspMI      aviII/fspI      hindIII      bsrDI
1201 CTCGGTTGCC GCCGGCGCTT TTTTATTGTT GCGAGCGGC ATCTCGAATG AACTGTGTC GCAGGTAGAA GCTTTGGAGA TTATCGTAC TGCATGCTT
GAGCCACGCG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA
^end lambda t0 terminator

```

FIG. 23B

1301 CCGAATATGG CGCAAAATGA CCAACAGCGG TTGATTGATC AGGTAGAGG GCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG
GGGTATACC GCGTTTACT GGTGTGCGC AACTAATAG TCCATCTCC CCGGACATG CTCCATTTCG GGTACGGTC GTAAGGACTG CTGCTATGCC bsmI

1401 AGCTGCTGG CGATTACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG CTGTCAATAA GTTGTACGG CCGAGACTTA
TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGAGG AGCAGTCATT TTTCAATTAG AAAAGTTGTC GACAGTATT CAACAGTGCC GGTCTCTGAAT pvuII eagI/xmaIII/ecI XI

1501 TAGTGGCTTT GTTTTATTT TTTAATGTAT TTGTAAGTAG TACGCAAGTT CACGTAAAAA GGTATCTAG AATTATGAAG AAGAATATCG CATTCTTCT
ATCAGCGAA CAAAAATAA AAATTACATA AACATTGATC ATCGTTTCAA GTGCATTTT CCCATAGATC TTAATACCTT TCTTATAGC GTAAAGNAGA xbaI
M K K N I A F L L
^STII Signal TIR-1

1601 TGCATCTATG TTGTTTTTT CTATTGCTAC AAACGGCTAC GCTCAGGTC AGCTGGTGA GTCTGGCGCA GAGGTGAAAA AGCCAGGGGC TTCAGTTAAA
AGGTAGATAC AAGCAAAAA GATAACGATG TTTGGCGATG CGAGTCCAAG TCGACCAAGT CAGACCGGT CTCCACTTTT TCGGTCCCG AAGTCAATTT
10 A S M F V F S I A T N A Y A Q V Q L V Q S G A E V K K P G A S V K
^start xVEGF(VNERK) heavy chain (consensus subgroup I framework
^FR1=SubgroupI

43 V S C K A S G Y T F T N Y G I N W V R Q A P G Q G L E W M G W I N T
^FR2=SubgroupI

1701 GTATCTCTGA AGCTTCTGG CTATACCTTC ACCAAGTATG GTATAAAGTGT GTCTGGTGCAG GCCCGGGTGC AGGGCTTGA ATGATGGA TGGATTAAAC
CATAGGACAT TTCAAGACC GATATGGAAG TGGTTGATAC CATATTGAC CCAGGCAGTC CCGGGCCCG TCCCGGACCT TACCTACCT ACCTAATTGT
77 Y T G E P T Y A A D F K R R V T I T A D T S T S T A Y M E L S S L
^FR3=SubgroupI

1801 CCTATACCG TGAACCGACC TAGTCTCGG ATTCAACG TAGTGTACT ATCACTGCTG ACACCTCCAC TAGCACAGCA TACATGGAAC TGTCTAGCT
GATATGCGC ACTTGGCTGG ATACGACGCC TAAAGTTTC AGCAATGA TAGTGACGAC TAGTGAGGTG ATCGTGTGCT ATGTACCTTG ACAGATGGA
77 Y T G E P T Y A A D F K R R V T I T A D T S T S T A Y M E L S S L
^FR3=SubgroupI

1901 GCGCTCTGAG GACATGCGG TCTATTACTG TGCAGCTTAC CCGCACTATT ATGTGAACGA CGGAADAGC CACTGGTATT TCGACGCTG GGGTCAAGGA
CGGAGACTC CTGTGACGC AGATAATGAC AGTGCATG GCGGTGATAA TACACTTGT CCGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT
110 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G
FR4= same sequence for subgroupI, II and III

2001 GCGCTCTGAG GACATGCGG TCTATTACTG TGCAGCTTAC CCGCACTATT ATGTGAACGA CGGAADAGC CACTGGTATT TCGACGCTG GGGTCAAGGA
CGGAGACTC CTGTGACGC AGATAATGAC AGTGCATG GCGGTGATAA TACACTTGT CCGCTTCTCG GTGACCATAA AGCTGCAGAC CCCAGTTCCT
110 R S E D T A V Y Y C A R Y P H Y Y V N E R K S H W Y F D V W G Q G
FR4= same sequence for subgroupI, II and III

FIG. 23C

bseRI
 esp3I
 bseRII bsmBI
 bspOMI/bsp120I
 apaI
 bbsI
 bseRI
 2001 ACCCTGGTCA CGTCTCTTC GGCCTCCACC AAGGCCCAT CGTCTTCCC CCTGGCACCC TCCTCCAGA GCACCTCTGG GGGCACAGCG GCCCTGGGCT
 TGGGACCACT GGCAGAGGAG CCGAGGTGG TTCCCGGTA GCCAGAGGG GGACCGTGG AGGAGTTCT CGTGGAGACC CCGTGTGCG CGGACCCGA
 143 T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A L G C

ecoNI
 ageI
 pflFI
 tth111I/aspI
 nari
 kasi
 eheI
 apaLI/snoI
 alw44I/snoI
 eco81I
 bsu36I/mstII/sau
 2101 GCTGTGTCAA GGACTACTTC CCGAACCAG TGAAGGTGTC GTGAACCTCA GGGCCCTGA CCAGCGGGGT GCACACCTTC CCGGTGTCC TACAGTCTC
 CGGACCACTT CTGATGAAG GGGCTTGGC ACTGCCACAG CACTTGAGT CCGCGGACT GGTGCCGCA CGTGTGAAG GCGCGACAGG ATGTCAAGAG
 177 L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q S S

alwNI
 alw26I/bsmAI
 ahdI/eam1105I
 earI/ksp632I
 bpuAI
 bbsI
 2201 AGGACTCTAC TCCCTCAGCA GCGTGTGAC TGTGCCCTCT AGCAGCTTGG GCACCCAGAC CTACATCTGC AACGTGAATC ACAAGCCCAG CAACACCAAG
 TCCTGAGATG AGGAGTCTT CGCACCACTG ACACGGGAGA TCGTGAAC CGTGGTCTG GATGTAGACG TTGCACCTAG TGTTCGGTC GTTGTGTTT
 210 G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N T K

rcaI
 bspHI
 eco81I
 bsu36I/mstII/sauI
 btri
 bbsI
 bpuAI
 eco81I
 2301 GTGGACAAGA AAGTTGAGCC CAATCTTGT GACAAAATC ACACATGCC ACCGTGCCA GCACCTGAAC TCCTGGGGG ACCGTGATC TTCTCTTCC
 CACCTGTCT TTCAACTCG GTTTAGAACA CTGTTTGG TGTGTACGG TGGACGGGT CGTGGACTTG AGGACCCCG AGGACAGTCAG AAGGAGAAGG
 243 V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V P L P P

drdI
 bpuAI
 eco81I
 bbsI
 bsu36I/mstII/sauI
 2401 CCCCACCAACC CAAGGACACC CTCATGATCT CCGGACCCC TGAGGTGACA TGCGTGTGG TGGACGTGAG CCACGAAGAC CCTGAGGTCA AGTTCAACTG
 GGGGTTTGG GTTCTCTGG GAGTACTAGA GGGCTGGG ACTCCAGTGT ACGCACACC ACCTGCACTC GTGCTTCTG GGAATCCAGT TCAAGTTGAC
 277 P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K P N W

sacII/sstII
 kspI
 bseRI
 bsgI
 ecoNI
 2501 GTACGTGGAC GCGGTGAGG TGCATATGC CAAGACAAG CCGGGGAGG AGCAGTACAA CAGCAGTAC CAGTGTGTC CGTGTCTCAG CCGTCTGAC
 CAGCACTG CCGCACCTCC AGTATTACG GTTCTGTTT CCGGCCCTCC TCGTCACTT TCGTGTGATG GCACACCACT CCGAGGAGT GCGAGAGTG
 310 Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H

bsaI
 2601 CAGGACTGGC TGAATGGCAA GGAGTACAG TGAAGGTCT CCAACAAAGC CCTCCAGCC CCATCAGA AAACATCTC CAAAGCCAA GGGCAGCCCC
 GTCCTGACCG ACTTACCGT CCTCATGTT CAGTTCAGA GGTGTTTTC GGAGGTGCG GGTAGTCT TTTGTAGAG GTTTCGGTT CCGTCTGGG
 343 Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G Q P R

FIG. 23D

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xmaI/pspAI      bspI407I/bsrDI      sexAI      bspMI      bspMI
2701 GAGAACACCA GGTGTACACC CTGCCCCCAT CCGGGAAGA GATGACCAAG AACGAGGTCA GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT
CTCTTGCTGT CCACATGTG GACGGGGTA GGGCCCTTCT CTACTGGTTC TTGTGCCAGT CGGACTGGAC GGACCAGITT CCGAAGATAG GGTGCTGTGA
377 E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S D I

berDI
2801 CGCCGTGGAG TGGGAGGCA ATGGGAGCC GGAGAACAAC TACAAGACCA CGCCTCCGT GCTGGACTCC GACGGCTCCT TCTTCTCTA CAGCAAGCTC
GGGCACTC ACCCTCTCT TACCGTGG CCTCTTGTG ATGTTCTGGT GCGGAGGCA CGACCTGAGG CTGCCGAGGA AGAAGGAGAT GTGCTGGAG
410 A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S K L

bpuAI      ppulOI      nsII/avaIII      bspI      earI/ksp632I
2901 ACCGTGACCA AGAGCAGGTG GCAGCAGGG AACGTCTTCT CATGCTCCGT GATGATGAG GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT
TGGCACCTGT TCTGTCCAC CGTGTCCC CGTGTCCC TTGCAAGA GTACGAGGCA CTACGTACTC CGAGACGTGT TGGTGTGTG CGTCTTCTCG GAGAGGACA
443 T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S

sphi      hpaI      bspDI      clai/bsp106
3001 CTCGGGTAA ATAAGCATGC GACGGCCCTA GAGTCCCTAA CGCTCGGTG CCGCCGGCG TTTTATTG TTAATCATG TTTGACAGCT TATCATCGAT
GAGGCCCAT TATTCGTACG CTGCCGGAT CTCAGGAT GCGAGCCAAC GCGGCCCGC AAAAATAAC AATTGATAC AAATGTCTGA ATAGTAGCTA
477 P G K O      ^lambda to terminator

hindIII      hpaI      bspDI      clai/bsp106
3101 AGCTTTAAT GCGTAGTTT ATCAGATTA AATTGCTAAC GCAGTCAGC ACCGTGTATG AAATCTAACA ATGCGTCTAT CGTCATCTC GGCACCGTCA
TTGGAATTA CGCATCAA TAGTCTAAT TTAACGATTG CGTCAGTCCG TGGCACATAC TTAGATTGT TACCGAGTA GCAGTAGGAG CCGTGGCAGT

ecorV
3201 CCTGGATGC TGTAGGCATA GGCTTGTGTTA TGCCGGTACT GCGGGCCTC TTGCGGGATA TCGTCCATC CGACAGCATC GCCAGTCACT ATGGCGTGTCT
GGGACCTACG ACATCGTAT CCGAACCAAT ACGGCCATGA CCGCCCGGAG AACGCCCTAT AGCAGGTAAG GCTGTCTAG CCGTCACTGA TACCGCACGA
3301

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FIG. 23E

> length: 3300

aatII (GACGTC):	1983
acc65I (GGTACC):	795 1176
ageI (ACCGGT):	1806 2126
ahaIII (TTTAAA):	590
ahdI (GACNNNGTC):	346 1495 2380
alw26I (CAGNNCTG):	1089 1770 2359
alw44I (GTGCAC):	1930 2169